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Datasheet for the decision of 30 January 2020

Case Number: T 0938/14 - 3.3.08

Application Number: 08157036.8

Publication Number: 2019316

IPC: C12N5/07

Language of the proceedings: EN

Title of invention:
Ex vivo human skin model

Patent Proprietor:
Symrise AG
Cutech S.R.L.

Opponents:
BASF Beauty Care Solutions France SAS
Dr. Füchsle Kathrin

Headword:
Ex vivo human skin model/SYMRISE AG, CUTECH SRL

Relevant legal provisions:
EPC Art. 113(1), 123(2), 54, 56, 83, 104(1)
RPBA Art. 12(4), 13

Keyword:

New main and auxiliary requests 1 and 3 - admitted (no)
Late-filed evidence - admitted (no)
Auxiliary request 2 - admitted (yes)
Auxiliary request 2 - inventive step - (no)
Apportionment of costs - (no)

Decisions cited:

T 0094/82, T 0252/02, T 0466/05, T 0288/06, T 0815/07

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Case Number: T 0938/14 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 30 January 2020

Appellant: (Patent Proprietor 1)	Symrise AG Mühlenfeldstrasse 1 37603 Holzminden (DE)
Appellant: (Patent Proprietor 2)	Cutech S.R.L. Via San Marco, 9/M 35129 Padova (IT)
Representative:	Fabry, Bernd IP2 Patentanwalts GmbH Schlossstrasse 523 41238 Mönchengladbach (DE)
Respondent: (Opponent 1)	BASF Beauty Care Solutions France SAS 32, rue Saint-Jean-de-Dieu 69007 Lyon (FR)
Representative:	Mendelsohn, Isabelle Cabinet Beau de Loménie 158, rue de l'Université 75340 Paris Cedex 07 (FR)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 19 February 2014 revoking European patent No. 2019316 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman	B. Stolz
Members:	D. Pilat
	J. Geschwind

Summary of Facts and Submissions

I. European patent N° 2 019 316 is based on European patent application N° 08 157 036.8 hereinafter "the patent application" and was opposed on the grounds of Articles 100 (a) and (b) EPC. The opposition division considered the main request filed on 15 November 2013 to meet the requirements of Articles 123(2)(3), 84 and 54 EPC but not those of Article 56 EPC. Accordingly, the patent was revoked.

II. With the statement of grounds of appeal, the appellant filed a new main request, a new auxiliary request and new documentary evidence D25.

III. In reply thereto, the opponent (respondent) maintained the objections raised under Article 123(2)(3), 83, 54 and 56 EPC against the main request and the auxiliary request.

IV. In reply to the respondent's submissions, the appellant filed new auxiliary requests 2 and 3.

V. The respondent submitted further arguments.

VI. The parties were summoned to oral proceedings. In a communication pursuant to Article 17(1) RPBA 2007, the parties were informed of the board's provisional, non-binding opinion on some of the legal and substantive matters of the case.

VII. In reply to the board' communication, the appellant, without providing substantive arguments, announced that it would not attend the oral proceedings.

VIII. Oral proceedings before the board were held on 30 January 2020, in the absence of the appellant.

IX. Independent claim 1 of the main request reads as follows:

"1. A method of modelling, simulating or analysing a selected effect of a selected treatment of human or animal skin, comprising the steps of:

(a) providing a skin sample of abdomen, thigh or breast of a human, the sample including an epidermis, dermis and a subcutis layer, said subcutis layer having an average thickness of 0,5 to 5 mm,

(b) subjecting the sample to the selected treatment, and

(c) observing one or more effect of the treatment on the skin sample, for the assessment of:

- modulation of fat metabolism,
- anti-cellulite properties of substances,
- anti-aging effects, particularly by fat cell stimulation
- allergenic potential and/or irritation,
- effects caused by mechanical stress as e.g. abrasion or pressure
- modulation of connecting-tissue properties, particularly for the assessment of anti-wrinkle properties of substances,
- modulation of skin barrier function,
- modulation of ion channels, especially neurofunctional channels and preferably channels activated by GABA, glutamate, acetylcholine, serotonin, adrenalin and ATP, and temperature

sensitive channels (TRPM8, TRPV3, TRPV4, TRPV1, ANKTM/TRPA1, TRPV2),
- immunestimulation, immunesuppression,
- sebum stimulation, sebum suppression,
- anti-microbial effectiveness, particularly anti-acne effectiveness,
- sweat secretion decrease,
- substantivity of materials on a skin surface,
- film forming effectiveness,
- modulation of skin and hair thickness,
- moisturization,
- phototoxicity,
- skin metabolism
- penetration properties
- release properties from formulations

of compounds.

Dependent claims 2 to 7 define specific embodiments of the method of claim 1.

X. The auxiliary request 1 is identical to the new main request except for the incorporation of the technical feature of claim 3 limiting step (a) of the method to a skin sample of abdomen of a human.

Dependent claims 2 to 6 define specific embodiments of the method of claim 1.

XI. The auxiliary request 2 is identical to the main request underlying the decision under appeal. It differs from the main request in step (c) which reads:

"(c) observing **the** effect of the treatment ...." (emphasis added).

Dependent claims 2 to 7 define specific embodiments of the method of claim 1.

XII. The auxiliary request 3 is identical to the the main request underlying the decision under appeal except for the incorporation of the technical feature of claim 3 limiting step (a) of the method to a skin sample of abdomen of a human.

Dependent claims 2 to 6 define specific embodiments of the method of claim 1.

XIII. The following documents are cited in this decision:

D4 La lettre d'information du Centre de Recherches Biologiques et d'Experimentations Cutanées (Laboratoire BIO-EC), La lettre d'information n°2, January 2003;

D7 M.-A. Bolzinger et al., 2008, European Journal of Pharmaceutics and Biopharmaceutics, vol.68, pages 446-451;

D18 P. Agache, 2004, "The Human Skin: An Overview", Chapter 1, pages 3 to 5, in: P. Agache and P. Humbert "Measuring the Skin", Springer Verlag;

D22 Muriel Isoir, soutenance le 7 June 2006, "Evaluation d'un modèle alternatif de peau dans l'étude de l'atteinte épidermique après exposition à différents agents de stress environnementaux: rayonnements ionisants (RI) et ultra-violets B (UVB)", Thèse de doctorat de l'Université de Versailles Saint-Quentin-en-Yvelines, pages 1-207;

D23 A. Laurent et al., 2007, Vaccine, vol. 25, pages 6423-6430;

D25 Prof. Giovanni Abatangelo, Expert Opinion on Human Skin Thickness, pages 1-7.

XIV. The appellant's written submission, insofar as relevant to the present decision, may be summarized as follows:

Admission of the new sets of claims submitted by the appellant and of document D25

Claim 1 of the new main request was based on claims 3, 7 and 10 as granted, except for the incorporation of the technical feature of "one or more" effects in step c) introduced for clarification. Claims 2 to 7 were based on claims 4 to 9 as granted with the dependencies adjusted. Auxiliary request 1 differed from the main request in that claim 1 step a) was limited to a skin sample of abdomen as in dependent claim 3. Auxiliary requests AR2 and AR3 were filed in response to the respondent's comments on the statement of grounds of appeal. Both auxiliary requests AR2 and AR3 corresponded to the new main and auxiliary request AR1 but for the "one or more" that was replaced by the granted "the" in step c) of claim 1.

The new main request was essentially the same as the main request of the decision under appeal which was found to meet the requirements of Articles 123(2) and 84 EPC during oral proceedings in opposition. Auxiliary requests AR1 to AR3 were slightly amended versions thereof.

Document D25 was filed to invalidate the novelty objection based on document D22, which disclosed a skin

sample having an average skin thickness of 5 mm and thereby implicitly and invariably a subcutis layer having the average thickness range of claim 1. Document D25 showed that a human male skin sample consisting of an epidermis and dermis could have a thickness of more than 5 or 6 mm. The novelty objection which inferred the presence of a subcutis layer in a skin sample having a thickness of 5 mm (see document D22) was therefore invalid.

No submissions were made in response to the preliminary non-binding opinion of the board concerning the late filing of both the new main request and auxiliary requests 1 to 3 as well as with regard to document D25.

Article 83 EPC

An objection of lack of sufficiency of disclosure was never raised before and thus lacked a proper basis. There was furthermore no difficulty for a skilled person to measure the thickness of a skin sample in light of the technical teaching provided in several documents cited in the opposition proceedings, e.g. using microscopy.

Article 54 EPC

The decision under appeal, point 7.3.3, was correct in concluding that document D22 disclosed all the features of steps a) and b) but not the specific effects listed in step c).

Article 56 EPC

Document D22 was considered to be the closest prior art.

It solved the problem of determining the performance of two different molecules (PP and GGA) as antioxidants in fighting skin damage caused by UV radiation using a skin sample of undefined composition. It did not address the problem of assessing different effects on skin attributed to effect-causing compounds, including effects on skin explants not found in two layer models; it did not provide either a skin model with improved viability and prognostic value.

There was no disclosure in document D22 of a three layer skin model as claimed in claim 1. There was no proof either that any skin sample with an average thickness of 5 mm included necessarily a subcutis because the thickness of an epidermis/dermis could not go beyond 5 mm. In the past, the subcutis layer was usually removed from the skin models, as it represented an inhomogeneous mixture of connective tissue and fat cells containing also follicle roots, nerves and veins, and had a negative impact on the test results. The subcutis tissue was furthermore more difficult to culture and caused permeation problems. For all these reasons the "full thickness models" of human skin had to refer to dermis + epidermis only. Thus, document D22 disclosed an undefined - probably a two-layer - skin model useful for assessing a couple of effects on skin or inside skin.

The objective problem underlying the present invention and document D22 was the same and could be formulated as in [0007] of the patent.

The skilled person faced with the technical problem of the present invention had neither a motivation nor a reasonable expectation of success to modify the

teaching of document D22, i.e. to use a three layered skin explant sample, as there was no pointer in document D22 to do so and because of prejudices in the prior art. The skilled person would therefore have been deterred from modifying the disclosure of document D22 to arrive at the subject-matter of claim 1 in an obvious manner.

XV. The respondent's submission, insofar as relevant to the present decision, may be summarized as follows:

Admission of the new sets of claims submitted by the appellant

In its reply to the notice of opposition, the patent proprietor/appellant submitted a first and a second auxiliary request that, in reply to a communication from the opposition division, were subsequently withdrawn and replaced by a new main request. This new main request was the sole request underlying the decision under appeal. The patent proprietor was asked by the chairman of the opposition division, at the end of the oral proceedings, whether he "wanted to file a last request in order to overcome the inventive step objection" to which it answered that he had no further request (point 7 of the minutes of the oral proceedings).

With the statement of grounds of appeal, appellant submitted a new main request, effectively replacing the main request underlying the decision under appeal and a new auxiliary request. The requests were not identical to the main request underlying the decision under appeal. The method of claim 1 step c) of both new requests was amended to "observing one or more effect [...]" instead of "observing the effect [...]". These requests were late filed and could have been filed

earlier during opposition proceedings. They should not be admitted into the appeal proceedings under Article 12(4) RPBA 2007.

The arguments submitted for the main and auxiliary request 1 above applied to the new auxiliary requests 2 and 3 submitted with appellant's letter dated 23 February 2015. These claim requests were not filed with appellant's statement of grounds of appeal as required under Article 13(1) RPBA 2020, and should not be admitted into the appeal proceedings.

Admission of document D25

Document D22 was filed in reply to the summons to oral proceedings in opposition proceedings, which the opposition division held pertinent (see appellant's letter dated 5 December 2013 in opposition proceedings). Document D25 was filed as an expert opinion to support appellant's arguments that document D22 did not implicitly disclose a three layer skin model having a subcutis layer having an average thickness of 0,5 to 5 mm and as such could not deprive the subject-matter of claim 1 of novelty.

Document D25 enclosing experimental evidence could have been filed earlier, i.e. in opposition proceedings, and contained references to documents which were not filed with appellant's statement of grounds of appeal. This document should therefore not be admitted into the appeal proceedings.

Article 123(2) EPC

Amended claim 1 contained added matter, because the list of effects to be assessed was shorter than the

list of effects originally mentioned in claim 10 and page 7 line 1 - page 8 line 21 of the patent application, while they were always and only mentioned all together, as a whole. Thus, claim 1 and its dependent claims contravened Article 123(2) EPC.

Article 83 EPC

The characteristics specified as essential for the alleged invention were not sufficiently disclosed or defined in the patent so as to enable the person skilled in the art to reproduce the claimed invention. The guidelines for examination and decision T 94/82 had to be applied (i.e. use of parameters).
The patent neither described a method of measuring the thickness of the subcutis layer nor defined or explained how it could be measured and how the "average thickness of the subcutis layer" was evaluated (see Decision T 252/02, reason 2.2). There was no example or reference method in the patent describing how this parameter was determined and how many different sites had to be measured in order to calculate said average thickness. The skilled person could not establish whether a skin explant sample fell under the scope of claim 1, which left the skilled person in doubt as to whether the skin explant used would solve the technical problem of the invention or not (see decision T0466/05; T0815/07; T0288/06).

Article 54 EPC

Document D22 anticipated the method of claim 1. It disclosed a method of analysing a selected antioxidant activity (i.e. selected effect) of catalase and glutathione peroxidase or an induction of the expression of HSP27 or HSP70, in a skin sample

subjected to UVB irradiation with a pre- or post-treatment either with Trolox or Polyphenol P or with Trolox or GGA respectively (i.e. selected treatment) (see pages 185 and 197 "Protocole expérimental"); Therefore testing a molecule for its protective effect against UVB, as it had been done for Polyphenol P and GGA, corresponded to observing the anti-aging effect of these molecules (see page 48 first paragraph).

The counting of sun burn cells was carried out to determine the extent of the UVB phototoxicity on the cells. The UVB phototoxicity could also be detected by assessing the level of UVB stress-induced immunolabelled heat shock proteins HSP27 and HSP70 whose expression was also known to be induced by mechanical stress (see document D22 pages 185 a), 197 a),c) and page 202). The anti-oxidant and heat shock protective activities of Trolox, Polyphenol P or GGA were shown to have an effect on skin metabolism. Thus, claim 1 lacked novelty.

Article 56 EPC

Document D22 represented the closest prior art for the subject-matter of claim 1.

Alternatively, in case the board did not consider document D22 to implicitly disclose a skin explant comprising a subcutis layer having an average thickness as defined in claim 1, document D7 represented the closest prior art.

The respondent agreed with the reasons given in point 8.3 of the decision under appeal.

Apportionment of costs

The board expressed a provisional opinion favourable to the position of the respondent in its communication. The appellant did not file any substantive reply, did not withdraw its request for oral proceedings, but with a letter dated 24 January 2020, the signer who neither signed the notice of appeal nor the statement of the grounds of appeal informed the board that she would not attend oral proceedings. Since appellant did not have the courtesy to inform the respondent's representative, the respondent, upon being informed of appellant's letter by the board's registrar, considered it unclear whether the patentee's representative will attend or not the oral proceedings. This behaviour amounted to an abuse of procedure because the respondent's representative had no other choice than to prepare the case and to attend oral proceedings.

XVI. The appellant requested the decision under appeal to be set aside and the patent to be maintained on the basis of the main request or any of auxiliary requests 1 to 3.

XVII. The respondent requested the appeal to be dismissed and apportionment of the costs incurred for attending the oral proceedings. It requested further that the main request and auxiliary requests 1 to 3 not be admitted into the appeal proceedings.

Reasons for the Decision

Article 113(1) EPC

1. By its decision not to attend the oral proceedings and not to file substantive arguments in reply to the issues raised in the board's communication, the

appellant has chosen not to make use of the opportunity to comment on the board's provisional opinion, either in writing or at oral proceedings, although this opinion was to the appellant's disadvantage. According to Article 15(3) RPBA 2020, the board is not obliged to delay any step in the proceedings, including its decision, by reason only of the absence at the oral proceedings of any party duly summoned who may then be treated as relying on its written case.

1.1 This decision is based on the same grounds, arguments and evidence on which the provisional opinion of the board was based.

Admission of the new main request and of auxiliary requests 1 to 3 submitted by the appellant.

2. Claim 1 of the new main request and of the auxiliary request 1 comprises a modified step c) which reads "observing one or more effect [...]", whereas the corresponding step c) in claim 1 of the main request underlying the decision under appeal reads: "observing the effect [...]".

3. As stated in point 10 of the board's provisional communication sent in preparation for the oral proceedings pursuant to Article 17(1) RPBA 2020 the board is not aware of any circumstances that may have prevented the appellant from submitting the new main claim request, effectively replacing the main request underlying the decision under appeal, and auxiliary request 1 during opposition proceedings. Nor has the appellant put forward any reasons for the late filing of these requests.

4. Moreover, according to the appellant, the amendment introduced into claim 1 of both the new main request

and auxiliary request 1 had the purpose to clarify the subject-matter claimed. However, an amendment aiming at only clarifying the subject-matter of a claim cannot be considered to be occasioned by a ground of opposition within the meaning of Rule 80 EPC. For this reason alone, both requests cannot be admitted into the proceedings.

4.1 The board decides not to admit the main request and auxiliary request 1 into the appeal proceedings.

5. According to Article 13(1) RPBA 2020, admission of late filed auxiliary requests 2 and 3, filed in response to respondent's submissions, is at the discretion of the Board.

6. Auxiliary request 2 is identical to the main request underlying the decision under appeal. This request has been implicitly withdrawn upon submission of a new main request and auxiliary request 1 with the statement of grounds of appeal and only later been reintroduced.

No justification was offered for the late re-introduction of auxiliary request 2.

In view of the circumstances of the case, the board decides, as an exceptional discretionary measure, to admit appellant's second auxiliary request into the appeal proceedings, as this allows it to review the decision under appeal.

7. Since no justification was given by the appellant why auxiliary request 3 could not have been filed earlier, the board makes use of its discretionary power and decides not to admit auxiliary request 3 into the proceedings (Article 12(4) RPBA 2007, Article 25(2) RPBA 2020).

Admission of document D25

8. With its statement of grounds of appeal, the appellant submitted document D25 as evidence in support of its argument that document D22 does not implicitly disclose a three layer skin model having a subcutis layer having an average thickness of 0,5 to 5 mm. Document D22 was consequently not capable of depriving the subject-matter of claim 1 of novelty.

9. The respondent objected to the admission of this new evidence into the proceedings because it was filed late and contained references to documents which had not been filed with the statement of grounds of appeal.

10. In its communication under Article 17(1) RPBA 2020, the board invited the parties to file observations on matters which it held to be of significance (see Rule 100(2) EPC and Article 15(1) and Article 17 RPBA 2020). The admission of the late filed document D25 was such an issue. Appellant did however not reply in substance to the board's communication. Nor are any compelling reasons on file why document D25 could not be filed earlier, i.e. during opposition proceedings.

The novelty objection based on document D22 had been raised in opposition proceedings with opponent's letter dated 5 December 2013 against which patentee had ample opportunity to react. Thus, the board does not admit document D25 into the appeal proceedings (Article 12(4) RPBA 2007). The same applies to any of the documents cited by reference in document D25.

Auxiliary request 2

Article 123(2) EPC - claim 1

11. The issue to be assessed is whether or not the list of effects in step (c) of claim 1, selected from of a longer list of effects mentioned in claim 10 and on page 7, line 1 to page 8, line 21 of the patent application, is directly and unambiguously disclosed in the patent application.

11.1 In claim 3, the patent application discloses a method of modelling, simulating or analyzing a selected effect of a selected treatment of human or animal skin, comprising the steps a) to c) of observing the effect of the treatment on the skin sample, while claim 10 depends on claims 3 to 9 and specifies that the method is for the assessment of a list of effects of compounds, all separated by a comma.

11.2 The board considers that the mere combination of features specified in claims 3 and 10 results in the subject-matter of step (c) of claim 1, except for the deletion of some listed properties of the effect-causing compounds.

Although the list of independent effects to be assessed in present claim 1 differs from the list of effects recited in claim 10 of the patent application, the deletion of specific and independent effects from a longer list of independent effects does not result in the singling out of a hitherto not mentioned group of effects but maintains the assessment of effects as a group differing from the original group by its smaller size only. Thus, the board confirms the findings of the

decision under appeal and concludes that claim 1 does not offend Article 123(2) EPC.

Article 83 EPC

12. The respondent contended that the characteristics specified as essential for the alleged invention were not sufficiently disclosed or defined in the patent to enable the person skilled in the art to reproduce the claimed invention. It referred especially to the guidelines for examination and decision T 94/82, as the average thickness parameter used in claim 1 was ill-defined.

12.1 The board notes that the EPO guidelines and decision T 94/82 of 22 July 1983, relate to the clarity of a claim and its scope of protection. However a lack of clarity is not a ground for opposition. It is therefore generally insufficient to establish a lack of clarity of the claims to establish an insufficiency of disclosure of the invention. It is furthermore up to the respondent to show that the patent as a whole does not enable the skilled person, relying on the description and on his common general knowledge, to carry out the claimed invention without undue burden. Thus, the identification of ill-defined parameters in the method of claim 1 is insufficient to conclude, absent any serious doubts substantiated by verifiable facts, that the claimed subject matter is insufficiently disclosed.

12.2 The decision T 252/02 of 7 December 2004, item 2.2.1, cited by the respondent, referred to a product characterized by unusual parameters. The skilled person was therefore not in a position to establish whether a product fell within the area covered by the claim and

to reliably prepare a claimed product characterized by a "cup crush peak load value" and a "cup crush energy value". None of the two parameters belonged to the skilled person's general knowledge and no standardized measurements to determine these parameters were known. One single measurement procedure was described in the patent specification, but no clear indications were given how multiple parameters affecting the measurement had to be selected. Under these circumstances, the skilled person was not in a position to establish whether the measured parameters could be effectively correlated to the claimed values. The subject-matter claimed was accordingly regarded as insufficiently disclosed within the meaning of Article 83 EPC (see item 2.2.5 of the decision).

12.3 The board considers the facts described in decision T 252/02 of 7 December 2004 not to be comparable with the facts of the present case. Firstly, the thickness of a subcutis layer cannot be viewed as an unusual parameter and secondly, several methods for determining the thickness of a tissue layer(s) were known in the prior art and readily available to the skilled person (cf. document D14, page 296, last paragraph to page 297, penultimate paragraph; document D12, paragraph 45.1.3, especially page 414, last paragraph, and document D23, Title). Even if different measurement methods lead to varying results, this does not prevent a skilled person from carrying out the invention. The average thickness of skins comprising a subcutis layer had been measured in the prior art by ultrasound imaging and was reported as the most accurate method for determining whole skin thickness largely independent of the experimental conditions used (see document D12, page 414, last paragraph and pages 415 and 416 bridging paragraph; document D14 second full

paragraph on page 297; document D23, abstract and Table 5). This rationale is applicable to the estimation of the "average" thickness, which can only stand for an arithmetic mean, a mid-range or a median.
Even if the variability resulting from the use of different methods may have an impact on the scope of protection provided by the claim, the mere absence of a reference to a specific method for measuring the thickness does not prevent the skilled person from carrying out the claimed invention. This stands in clear contrast to the cases underlying decisions T 466/05 of 19 December 2006, T 288/06 of 23 October 2009 and T 815/07 of 15 July 2007 where no method for reliably measuring a parameter could be identified and where the level of uncertainty of the values measured was high.

12.4 In the board's view, the respondent's objections rather concern the clarity of the definition of the claimed subject matter. The estimated thickness of the subcutis skin layer may vary slightly depending on the method of measurement and on the type of calculation of the mean (Article 84 EPC).
Lack of clarity is however not a ground for opposition and cannot be raised against a feature that was present in granted claim 1 and remained unamended in current claim 1 (see decision G 3/14, OJ EPO 2015, 102). Thus, the board concludes that the requirements of Article 83 EPC are met. The same conclusion applies to claims 2 to 7 dependent thereon.

Article 54 EPC

13. The respondent argued that document D22 disclosed a method of analysing a selected antioxidant activity (i.e. selected effect) of catalase, glutathione

peroxidase and superoxide dismutase or an induction of the expression of HSP27 or HSP70, in a skin sample subjected to UVB irradiation with a pre- or post-treatment either with Trolox or Polyphenol P, or with Trolox or GGA, respectively (i.e. selected treatment) (see pages 185 and 197 "Protocole expérimental"). This corresponded to observing the anti-aging effect of these molecules (see page 48 first paragraph) or of the skin metabolism of compounds.

Document D22, on pages 197 c) and 202, disclosed that HSPs perform essential functions in cells and were essential for their survival during stress of chemical, physical or metabolic origin. HSP27 and HSP70 were immunolabelled. HSP27- or HSP70- immunopositive cells were then counted in skin explants treated with UVB in the presence or absence of GGA and Trolox. This experimental set-up rendered the assessment of effects caused by mechanical stress straightforward.

14. In the board's view, document D22 discloses the counting of sun burn cells after UVB treatment in the presence or absence of Trolox or Polyphenol P in the skin explant's culture medium (cf. pages 185 a) and 197 a)). This experiment indicates that an assessment of UVB induced phototoxicity was carried out which is however not assigned to a compound as required by claim 1.

14.1 The assessment of an antioxidant protective effect conferred by pre- or post- treatment of Trolox, Polyphenol P and GGA on UVB irradiated skin explants, cannot be equated with an assessment of anti-ageing effects of these compounds only, as it encompasses anti-photoinflammatory effects and/or anti-photoneoplastic effects as well.

14.2 Even if, following respondent's interpretation, a skilled person could assess effects of mechanical stress using the immunolabelled heat shock proteins, there is no direct and unambiguous disclosure on pages 197 to 202 of document D22 of the assessment of a mechanical stress, let alone of the mechanical stress of a particular compound.

14.2.1 Skin metabolism of compounds covers all the processes of biotransformation (metabolism) of compounds occurring in skin tissues. It includes the permeation processes of compounds, the metabolic activities of enzymes acting on the compounds and acting on their metabolized forms. Document D22 does however neither disclose that observing the catalase, glutathione peroxidase and superoxide dismutase activity nor of the cells immunopositive for HSP27 and HSP70 was carried out for the assessment of skin metabolism of Trolox, Polyphenol P or GGA or of any other compounds.

14.3 Thus, in line with the established case law of the Boards of Appeal, the generic disclosure of an antioxidant protective effect does not constitute a direct and unambiguous disclosure of observing the specific anti-ageing effect mentioned in claim 1, even if it is encompassed by the generic disclosure of document D22.
The counting of HSP27- or HSP70- immunopositive cells of skin explants that had been irradiated with UVB in the presence or absence of GGA and Trolox is nowhere used for the assessment of the mechanical stress of a compound as defined in claim 1 nor is the observation of catalase, glutathione peroxidase and superoxide dismutase activities or of cells immunopositive for HSP27 and HSP70 used for the assessment of skin

metabolism (i.e. biotransformation or permeation processes) of Trolox, Polyphenol P or GGA or other compounds either.

14.4 Thus, document D22 does not deprive claim 1 or any dependent claim of novelty.

Article 56 EPC

15. It is common ground that document D22 represents the closest prior art for the subject-matter of claim 1.

15.1 Document D22 relates to a method of analysing a selected antioxidant activity (i.e. a selected effect) of catalase, glutathione peroxidase and superoxide dismutase or an induction of the expression of HSP27 or HSP70, in a skin sample subjected to UVB irradiation with a pre- or post- treatment either with Trolox or Polyphenol P, or with Trolox or GGA, respectively (i.e. selected treatment)(see pages 185 and 197 "Protocole expérimental"). The human female skin explant BIO-EC model, obtained by abdominoplasty, comprising epidermis and dermis, was used to test the anti-oxidative capacity of Trolox, polyphenol P and geranylgeranylacetone (GGA) compounds (see also page 24, II.3, second paragraph; page 75, I.2.2, especially line 7; page 92, title; page 83, second paragraph and page 94, third paragraph; pages 185 and 197).

15.2 Appellant argued that document D22 did not disclose a human skin explant consisting of three layers. The skin samples with a thickness of 5 mm disclosed in document D22 could only contain an epidermis and a dermis layer. In the past, the subcutis was removed from the skin models because its presence rendered more difficult the skin explant culture and caused permeation problems.

The subcutis represented an inhomogeneous mixture of connective tissue and fat cells, containing follicle roots, nerves and veins, having a negative impact on the results obtained. For all these reasons, the so called "full thickness models" of human skin disclosed in document D22 referred most certainly to a skin explant consisting of only dermis and epidermis.

15.3 Document D23 reports the mean skin thickness (epidermis and dermis) at the waist, an abdominal area, of 205 women and 137 men as 1,91 mm (see abstract).
A textbook (document D18) describes the skin as a stratified tissue with four layers, consisting of stratum corneum (0,02 mm), the viable epidermis (0,1 mm) and dermis (1,1 mm) and the subcutis (0,1 mm to several cm). The average thicknesses of the outer first three skin layers add up to a thickness of 1,22 mm. These data indicate that a human skin sample with an overall thickness of 5 mm includes a subcutis layer with a thickness of approximately 3,8 mm. Both, the data of documents D23 and D18 confirm the presence of a subcutis layer having an average thickness as defined in claim 1. The extended viability of the skin explants for at least 12 days observed for the explants of the patent is equally reported in document D22 (see page 24, second paragraph; patent on page 2, [0011], lines 53-56).

15.4 Since the skin explants described in document D22, obtained from 30 to 40 years old healthy female humans of Caucasian type by abdominoplasty, had a thickness of 5 mm, these explants have to comprise a subcutis layer having an average thickness ranging from 0,5 to 5 mm (see document D22 page 75, I.I.2; Article of M. Isoir et al. in J. Dermatol. Sci. annexed after page 97, see Article page 56, second column paragraph 2.1).

15.5 Starting from document D22, the problem to be solved can be defined as the provision of a method for modelling a selected effect of a selected treatment of human skin, which allows the assessment of a huge variety of effects, is easy to use and has a high prognostic value (see [0007] of the patent).

15.6 As a solution to this problem, the patent proposes the method of claim 1.

15.7 It is uncontested that the method of claim 1 solves this problem.

15.8 Even if the board accepts that subcutis layers were removed from skin models in the past because they represent an inhomogeneous mixture of connective tissue and fat cells, containing follicle roots, nerves and veins and were considered to have a negative impact on the test results, were difficult to culture and caused permeation problems, this assessment cannot apply to the human skin explants used in document D22. Said skin explants necessarily comprised a subcutis layer having a thickness ranging between 0.5 and 5 mm and were maintained in culture for up to 12 days.

15.9 The difference between the method of document D22 and the method of claim 1 lies in that it refers to a step of observing the effect of the treatment on the skin sample for the assessment of a great number of effects (cf. item IX., above).

15.10 As the human skin explant in document D22 has been shown to have a subcutis layer with an average thickness ranging between 0,5 to 5 mm and said explant could be kept alive for 12 days, there was no need to

find a motivation to use a three layer human skin sample to solve the technical problem identified above.

15.11 Thus, based on the content of the closest prior art document D22, the objective technical problem is reformulated as the provision of a method of modelling, simulating or analysing a selected effect of a selected treatment of human or animal skin for the assessment of a further effect.

15.12 Document D22 suggests explicitly to use the human female abdominal skin explants for the assessment of effects of at least dermatological and cosmetic products on the morphology, structure and metabolism of skin and for the assessment of chemical aggression and sun exposure (see page 24, lines 10-12 and lines 20-21).

15.13 The use of the skin explant model for numerous assessments was considered straightforward in document D22 (see e.g. page 24, especially lines 1, 5-6, 12-14 and 19-23, page 92, lines 1-3, pages 185 and 197). The patent provides actually no experimental data and thus no evidence that the skilled person was expecting or had to overcome any technical problems when using a three layered skin model instead of a two layered model. Applying the same standard of skill, starting from document D22, a skilled person had no reason to be discouraged from, but was instead encouraged to use the three layered skin model for the applications explicitly specified in document D22 or for other closely related possible applications it would have recognized as forming part of the group of alternative solutions without particular skills.
In consequence no inventive activity can be acknowledged for solving the technical problem of

providing an alternative application for the use of a skin model, since the selection of the claimed alternative application is not justified by a hitherto unknown technical effect distinguishing it from the solutions proposed in the prior art.

15.14 The board concludes that a skilled person faced with the technical problem defined in point 15.11 above would have selected any of the other assessments disclosed in document D22 to solve the problem posed. The selection of skin irritation caused by chemical aggression or skin metabolism alteration occasioned by dermatological or cosmetic products, from among all the options disclosed in document D22, cannot be seen to involve an inventive activity.

15.15 Thus, the subject-matter of claim 1, and consequently auxiliary request 2, does not meet the requirements of Article 56 EPC.

Apportionment of costs

16. In opposition appeal proceedings the board may, for reasons of equity, deviate from the principle of each party bearing its own costs, and order their different apportionment (Article 104(1) in conjunction with Article 111(1), second sentence, Rule 100(1) EPC, and Article 16(1) RPBA 2020). Such reasons of equity exist, when a party's costs arise from culpable actions of an irresponsible or even malicious nature by another party (Case Law of the Boards of Appeal, 9th ed. 2019, III.R.2).

16.1 In the present case, both parties to the appeal proceedings had requested oral proceedings in case the board was not inclined to concur with their respective

positions. In the board's communication under Article 17 RPBA 2020, the board dealt with appellant's arguments in some detail, concluding that the appeal was likely to be dismissed. However, from the board's communication, it was clear that oral proceedings had to take place, as appellant's request to maintain a patent based on the main request could not be granted. Even if appellant's representative could have informed the respondent's representative, as a matter of professional courtesy, that it would not attend oral proceedings, as it did for the board, even though in a slightly ambiguous manner, the other party could have, on the other hand, made an attempt to ask for clarification. Thus, the board cannot see any culpable actions of an irresponsible or even malicious nature in appellant's letter that would justify an apportionment of costs incurred by the respondent for attending the oral proceedings.

Besides, the respondent stated that even though the board's preliminary opinion was in its favour, it held it necessary to attend oral proceedings in case the board changed its mind. The request for apportionment of costs is therefore rejected.

Order

For these reasons it is decided that:

The appeal is dismissed

The Registrar: The Chairman:

L. Malécot-Grob B. Stolz

Decision electronically authenticated