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Datasheet for the decision of 14 January 2025

Case Number: T 1791/22 - 3.3.04

Application Number: 14739842.4

Publication Number: 3024448

IPC: A61K31/11, A61P1/06, A61P1/00

Language of the proceedings: EN

Title of invention:
Compositions and methods using p-anisaldehyde

Patent Proprietor:
Société des Produits Nestlé S.A.

Opponent:
N.V. Nutricia

Relevant legal provisions:
EPC Art. 100(b), 83, 54, 56

Keyword:
Sufficiency of disclosure - after amendment
Novelty - (yes)
Inventive step (yes) - non-obvious alternative

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Case Number: T 1791/22 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 14 January 2025

Appellant: (Opponent)	N.V. Nutricia Eerste Stationsstraat 186 2712 HM Zoetermeer (NL)
Representative:	Nederlandsch Octrooibureau P.O. Box 29720 2502 LS The Hague (NL)
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Representative:	Strych, Sebastian, et al Mitscherlich PartmbB Patent- und Rechtsanwälte Karlstraße 7 80333 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 1 June 2022 rejecting the opposition filed against European patent No. 3024448 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairwoman	M. Pregetter
Members:	R. Hauss
	M. Blasi

Summary of Facts and Submissions

I. European patent No. 3 024 448 (patent in suit) was granted with a set of seven claims. Independent claim 1 reads as follows:

> *"1. A composition comprising a therapeutically effective amount of p-anisaldehyde for use to treat dysphagia."*

II. The patent in suit was opposed under Article 100(a) and (b) EPC on the grounds that the claimed subject-matter lacked novelty and inventive step and was not disclosed in a manner sufficiently clear and complete for it to be carried out by the person skilled in the art.

III. The patent proprietor requested that the opposition be rejected and the patent maintained as granted. It also filed auxiliary claim requests.

IV. The documents cited in the proceedings before the opposition division include the following.

D1: WO 2014/181724 A1 (in Japanese language)

D2: PatBase Machine translation of D1 into English

D3: PLOS ONE | DOI:10.1371/journal.pone.0127060, 11 pages (15 May 2015)

D4: Journal of Food Science 76(7), C1032-C1038 (2011)

D5: Muscular Dystrophy Association, ALS Division: "Meals for Easy Swallowing", 114 pages (2005)

D7: Br J Clin Pharmacol 62(3), 369-371 (2006)

D8: Gastroenterology Research and Practice (2011), Article ID 818979, DOI:10.1155/2011/818979, 13 pages

D9: Schulz et al., "Rational Phytotherapy", 4th edn. (2001), ISBN 978-3-642-98095-4, Chapter 4.3: "Herbal Cough Remedies" including sections 4.3.1 and 4.3.2

D10: ISRN Pharmaceutics, Article ID 510795 (2012); DOI:10.5402/2012/510795, 8 pages

D11: Foods 6, 73; DOI:10.3390/foods6090073 (2017), 11 pages

D12: Neuron 41, 849-857 (2004)

D14: J Pharmacol Sci 115, 99-104 (2011)

D15: Neuropharmacology 44, 958-967 (2003)

V. The decision under appeal is the opposition division's decision rejecting the opposition, announced on 28 June 2021 and posted on 1 June 2022.

VI. The opposition division's relevant findings in the decision under appeal were the following.

(a) The subject-matter of the claims as granted met the requirement of sufficiency of disclosure (Article 100(b) EPC).

(b) The claimed subject-matter was also novel relative to the disclosure of documents D1/D2 and D5 (Articles 100(a), 52(1) and 54 EPC).

(c) Inventive step was assessed starting from the disclosure of documents D7 and, alternatively, D8. In both cases, the objective technical problem was the provision of an alternative composition for use in the treatment of dysphagia, and the claimed subject-matter was found to involve an inventive step (Articles 100(a), 52(1) and 56 EPC).

VII. The opponent (appellant) filed an appeal against this decision.

VIII. With its reply to the statement setting out the grounds of appeal, the patent proprietor (respondent) filed 13 amended sets of claims as auxiliary requests.

IX. The board issued a summons to oral proceedings. In the accompanying communication under Article 15(1) RPBA, *inter alia*, the following points were mentioned.

- The board expressed its preliminary opinion that the subject-matter of the claims as granted was novel over the disclosure of D1/D2 and D5.
- The question arose whether D1 was even comprised in the state of the art under Article 54(2) or (3) EPC.
- The board was not convinced by the appellant's reasoning that the claimed subject-matter would have been obvious to the person skilled in the art.

X. Oral proceedings before the board took place on 14 January 2025, in accordance with the parties' requests. At the oral proceedings, the respondent withdrew auxiliary request 1, replacing it with an amended set of claims. The board admitted new auxiliary request 1 and ultimately found this set of claims allowable.

XI. Claim 1 of new auxiliary request 1 filed at the oral proceedings reads as follows:

> *"1. A composition comprising a therapeutically effective amount of p-anisaldehyde for use to treat oral pharyngeal dysphagia."*

The remaining claims 2 to 6 are dependent claims.

XII. The appellant's pertinent arguments may be summarised as follows.

Sufficiency of disclosure

The claimed effects of treating dysphagia (claim 1 as granted), treating oral pharyngeal dysphagia (claim 2 as granted and claim 1 of new auxiliary request 1) and provoking a swallowing reflex (claim 4 as granted and claim 3 of new auxiliary request 1) were not rendered credible in the application as filed. Firstly, provoking a swallowing reflex did not amount to actual, i.e. curative, treatment of dysphagia. Secondly, the application as filed provided *in vitro* data only and did not describe the relevant experimental set-up in sufficient detail. Post-published data presented in document D3 gave rise to further doubt about the alleged activity and effects of p-anisaldehyde. Thus, the claimed therapeutic effects were at least not credible across the entire breadth of the therapeutic use defined in the claims. Moreover, it would have presented an undue burden for the person skilled in the art to extrapolate *in vitro* findings of EC_{50} values to implement the clinical treatment of dysphagia in practice.

Admittance of new auxiliary request 1

The appellant did not object to the admittance of new auxiliary request 1.

Novelty

The subject-matter of all claims of the main request (claims as granted) lacked novelty over the disclosure of documents D1 and D5. The same arguments and conclusion applied to the claims of new auxiliary request 1.

Inventive step

The disclosure of D7 or D8 could be used as a starting point for the assessment of inventive step. In either case, the objective technical problem for claim 1 of auxiliary request 1 was the provision of an alternative compound for use in the treatment of oral pharyngeal dysphagia. The claimed subject-matter would have been obvious because p-anisaldehyde was present in plants and their essential oils that had been used previously for improving the ability to swallow or that also contained menthol (known from D7 for triggering the swallowing reflex). Moreover, it was reiterated that the alleged therapeutic effect was not achieved across the scope claimed and, in particular, that very high or very low amounts of p-anisaldehyde would not provide a therapeutic benefit for dysphagic patients.

XIII. The respondent's pertinent arguments may be summarised as follows.

Sufficiency of disclosure

The experimental *in vitro* data presented in the patent in suit (paragraphs [0027] to [0029] and Figure 7) and, correspondingly, in the application as filed sufficed to provide proof of concept of the claimed therapeutic use of p-anisaldehyde. The appellant had not provided any counter-evidence that could give rise to serious doubt substantiated by verifiable facts in this regard. Pharmaceutical development on the basis of promising *in vitro* data was a routine activity and, in the absence of specific obstacles, did not amount to undue burden on the person skilled in the art.

Admittance of new auxiliary request 1

New auxiliary request 1 was filed in response to a new objection presented at the oral proceedings before the board. This was an exceptional circumstance justifying the request's admittance under Article 13(2) RPBA. The new request addressed the objection by omitting the claim that had been objected to.

Novelty

None of the documents cited by the appellant against novelty disclosed, directly and unambiguously, the use of p-anisaldehyde as the active agent in the claimed therapeutic use of treating oral pharyngeal dysphagia.

Inventive step

The appellant's arguments on inventive step were based on the inherent presence of p-anisaldehyde in several essential oils. However, a prior-art use that, at best, might unintentionally have fallen within the use recited in the claims could not render the claimed subject-matter obvious. Starting from document D7, which disclosed that menthol triggered the swallowing reflex, the person skilled in the art would have had no incentive to investigate peppermint oil and its further components. Starting from document D8, which disclosed the activity of capsaicin and piperine as TRPV1 agonists, the person skilled in the art would have had no reason to investigate p-anisaldehyde or essential oils containing it as possible alternative agents.

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

XV. The respondent requested that the appeal be dismissed or, in the alternative, that the patent be maintained in amended form on the basis of the claims of new

auxiliary request 1, filed on 14 January 2024 during oral proceedings before the board or, in the further alternative, that the patent be maintained in amended form on the basis of the claims of one of auxiliary requests 2 to 13, all filed with the respondent's reply to the statement setting out the grounds of appeal.

Reasons for the Decision

1. Claim construction

1.1 Article 54(5) EPC provides that the patentability of a substance or composition comprised in the state of the art, for any specific use in a method referred to in Article 53(c) EPC, is not excluded, provided that such use is not comprised in the state of the art.

1.2 The treatment of dysphagia, or of oral pharyngeal dysphagia, meets the criterion of being a therapeutic method under Article 53(c) EPC. Hence, claim 1 as granted (see point I. above) and claim 1 of auxiliary request 1 (see point XI. above) are purpose-related product claims pursuant to Article 54(5) EPC.

1.3 In accordance with the claim format and special concept of patentability provided for in Article 54(5) EPC, the therapeutic indication "use to treat (oral pharyngeal) dysphagia" is a limiting technical feature that must be taken into account in the assessment of novelty and inventive step. The wording of claim 1 also implies that p-anisaldehyde is the pharmacologically active agent that provides the therapeutic effect.

1.4 For the requirement of sufficiency of disclosure to be met, the therapeutic efficacy of the claimed composition in respect of the stated therapeutic

indication must be credible. This means in the case at hand that the therapeutic efficacy of p-anisaldehyde has to be credible.

2. Main request - sufficiency of disclosure (Article 100(b) EPC)

2.1 The requirement of sufficiency of disclosure must be satisfied at the effective date of the patent, i.e. on the basis of the information provided in the patent application together with the common general knowledge then available to the skilled person.

2.2 The patent in suit and the application as filed set out that dysphagia is a condition characterised by a decreased ability to swallow.

The normal swallowing process involves three distinct, albeit interdependent, phases: the oral, the pharyngeal and the oesophageal phases.

In medicine, a distinction is made between oral pharyngeal dysphagia and oesophageal dysphagia. Oesophageal dysphagia, which is considered a less serious form of dysphagia, affects individuals of all ages and is treatable with medication. Oral pharyngeal dysphagia is more prevalent in older individuals, is generally not treatable with medication, and is considered a very serious condition in view of the danger of airway obstruction and pulmonary aspiration of liquids and semi-solid foods (see paragraphs [0002] to [0005] of the patent in suit and the corresponding paragraphs [0002] to [0005] of the application as filed).

2.3 The patent in suit and the application as filed relate to the treatment of dysphagia. This is to be

achieved by administering a composition comprising p-anisaldehyde to provoke a swallowing reflex.

2.4 The proposed mechanism of action involves the activation of the transient receptor potential cation channels TRPV1 and TRPA1 that are expressed in the somatosensory fibres innervating the oral cavity by contact with a composition comprising the active agent p-anisaldehyde (see paragraphs [0006] to [0009], [0027] and [0029] and Figure 7 in the patent in suit and the corresponding paragraphs [0006], [0007], [0015], [0058] and [0061] and Figure 7 in the application as filed).

2.5 On the basis of this mechanism, the treatment is supposed to help with initiating the swallowing process. This is consistent with addressing oral pharyngeal dysphagia.

2.6 However, claim 1 as granted is not restricted to the treatment of oral pharyngeal dysphagia but relates to the treatment of dysphagia in general. This broader term also includes oesophageal dysphagia.

2.7 The respondent maintained that patients suffering from oesophageal dysphagia would benefit inherently from the envisaged treatment because, as set out in paragraph [0002] of the patent in suit, the oesophageal phase of swallowing was involuntary and reflexive and would not occur without the oral and pharyngeal phases being triggered first.

2.8 This argument is not convincing. While the phases of swallowing are interdependent, the fact that the oesophageal phase can only follow the other two phases does not result in a mechanism enabling the treatment of oesophageal dysphagia. Patients with oesophageal dysphagia do not necessarily require support in initiating the oral and pharyngeal phases of the

swallowing process since these patients do not necessarily also suffer from oral pharyngeal dysphagia. Oesophageal dysphagia is a separate, independent disorder that typically results from different causes such as a motility disorder or obstruction at the level of the oesophagus. It is not apparent that the impairment of the oesophageal phase caused by such dysfunctions could be addressed by triggering the oral and pharyngeal phases of swallowing.

2.9 In conclusion, the respondent's explanation does not make it credible that the claimed composition can also treat oesophageal dysphagia. Hence, the subject-matter of claim 1 as granted does not meet the requirement of sufficiency of disclosure for the envisaged therapeutic use over the entire scope of the therapeutic indication "dysphagia" (see point 1.4 above).

2.10 As a consequence, the ground for opposition under Article 100(b) EPC prejudices the maintenance of the patent as granted.

3. Auxiliary request 1 - admittance (Article 13(2) RPBA)

3.1 The respondent filed the set of claims of new auxiliary request 1 at the oral proceedings before the board, in replacement of former auxiliary request 1 filed with the reply to the appeal.

3.2 The filing of a new set of claims constitutes an amendment of the appellant's appeal case. Based on the time of filing in the case at hand, the criteria of Article 13(2) RPBA apply for the admittance of new auxiliary request 1.

3.3 The amendment was occasioned by a new objection under Rule 80 EPC arising at the oral proceedings before the board against claim 2 of former auxiliary request 1.

3.4 The difference between former auxiliary request 1 and new auxiliary request 1 is that claim 2 has been deleted and the subsequent claims and their dependencies have been re-numbered accordingly. This amendment overcomes the objection under Rule 80 EPC.

3.5 In this situation, the board found that exceptional circumstances justified the filing of new auxiliary request 1 and decided to admit this request under Article 13(2) RPBA.

4. Auxiliary request 1 - sufficiency of disclosure (Article 83 EPC)

4.1 The use defined in claim 1 of auxiliary request 1 is to treat oral pharyngeal dysphagia. Auxiliary request 1 thus overcomes the objection against the main request considered in section 2. above.

4.2 In the section on the technical background, the application as filed sets out that capsaicin, a known agonist of the TRPV1 cation channel, had been shown to promote a swallowing reflex (see paragraphs [0006] and [0007]).

According to the section summarising the invention, the inventors found p-anisaldehyde to be an agonist of the cation channels TRPV1 and TRPA1 and believe that this activation of TRPV1 and TRPA1 is effective for helping provoke the swallowing reflex in dysphagic patients (see paragraph [0015] in the application as filed and point 2.4 above).

Furthermore, Figure 7 shows experimental data demonstrating that p-anisaldehyde activates TRPA1 and TRPV1, while no activation of hTRPM8 was observed. It is reported that p-anisaldehyde activated TRPA1 with an EC_{50} of about 100 µM and TRPV1 with an EC_{50} of about 500 µM (see paragraph [0058] of the application as filed). Figure 7 is presented as follows:

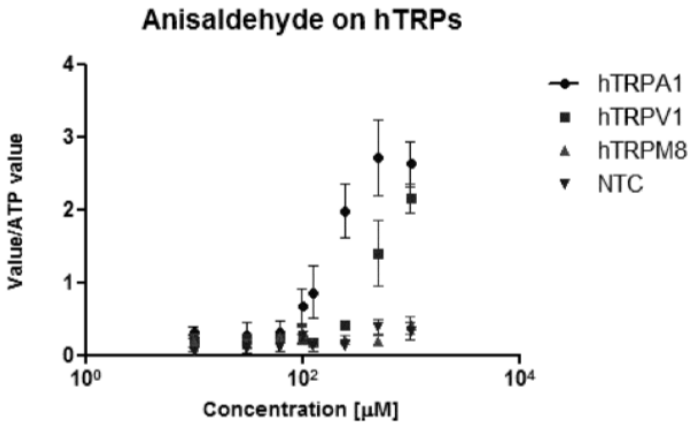

FIG 7.

4.3 Thus, the application as filed provides a mechanistic explanation for the alleged activity of p-anisaldehyde, corroborated by experimental *in vitro* data. The EC_{50} parameter indicates the concentration at which half the maximal effect of the agent is reached.

4.4 The appellant presented the following arguments in support of its objection that the claimed therapeutic efficacy had not been rendered credible.

(a) Provoking a swallowing reflex did not amount to actual treatment of the underlying condition of dysphagia.

(b) The experimental data provided in the patent in suit and in the application as filed did not make the claimed therapeutic use credible because the methodical set-up was not described in sufficient

detail to enable the person skilled in the art to reproduce these experiments and their results. The reported EC_{50} values were thus based only on assertion.

(c) Furthermore, the data provided was contradictory. The EC_{50} value for hTRPA1 as shown in Figure 7 could be estimated to be between 300 and 400 µM. As this differed from the value of 100 µM reported in the description, the evidence in the application as filed was not conclusive.

(d) The post-published document D3 contained evidence that raised further serious doubt about the experimental data presented in the patent in suit on the activation of both TRPV1 and TRPA1. According to D3, p-anisaldehyde had been tested for activation of hTRPV1 and hTRPA1 but had been found to not activate hTRPV1 and to be only a partial weak agonist of hTRPA1, with an EC_{50} of 546.5 µM.

(e) Proof of concept could in any case not be based on showing that p-anisaldehyde activated TRPA1 because it had not been common general knowledge at the relevant date that TRPA1 activation indeed promoted the swallowing reflex.

(f) The *in vitro* data in the application as filed could not show that a therapeutic window indeed existed for p-anisaldehyde, i.e. a dosage range in which a therapeutic benefit in patients could be attained without side effects, such as unpleasant sensations, that would preclude its use at a therapeutically effective dosage.

(g) Claim 1 of auxiliary request 1 did not restrict the claimed medical use to any particular route of administration. The claimed therapeutic efficacy

was not rendered credible across the entire scope of conceivable administration routes since no guidance was provided as to how it could be attained by routes other than oral administration.

4.5 These arguments do not succeed for the following reasons.

4.5.1 Regarding point (a)

In line with the established case law of the boards and contrary to the appellant's view, a treatment that lessens symptoms of a disorder falls under the concept of treatment by therapy. This reading of claim 1 is furthermore in line with the usual understanding of what is encompassed by the term "treatment" and also with the definition given in the patent in suit (see paragraph [0023]) and the application as filed (paragraph [0054]), according to which the term "treatment" includes measures that lessen symptoms of a diagnosed pathologic condition or disorder.

4.5.2 Regarding point (b)

The application as filed provides some relevant detail about the set-up of the experiment by which the EC_{50} data were obtained. According to paragraph [0051] (corresponding to paragraph [0020] of the patent in suit), Figure 7 shows the *in vitro* effect of p-anisaldehyde on cell expression of TRP channels. Thus, an *in vitro* cell model was used that was based on cells expressing the TRP cation channels of interest. According to Figure 7, the experimental measurements were based on ATP to reflect energy turnover as a measure for the activity of the expressed receptors in relation to the concentration of p-anisaldehyde.

The upshot is that the general principle of the experiment is indeed disclosed and that, based on this

information, the experiment is suitable for demonstrating the effect of p-anisaldehyde as an agonist of the TRP channels in question.

At the effective date, the person skilled in the art would have had the knowledge to perform experiments following this general principle to verify the alleged effect. This is corroborated by the fact that similar experiments are outlined in the prior art, without apparently requiring a particularly detailed description, and by reference to well-known techniques and available materials (see D12: page 856: "Experimental procedures"; D15: page 959, point 2.4 and page 961, point 3.2). While D12 and D15, as journal articles, do not represent common general knowledge, their disclosure on experimental methods nevertheless suggests that no difficulties were at the time encountered by researchers in setting up experiments on TRP activation.

The appellant failed to substantiate its further objection that crucial information was missing owing to the application not disclosing which cell line was used for the *in vitro* model. According to the appellant, the choice of cell line has an important impact on the test results. Without further substantiation, this argument remains speculative. The relevant characteristic of the cells of the *in vitro* model would seem to be not their origin and basic cell type but rather the fact that they express TRPA1 and TRPV1. Such cells were known and could be obtained by well-known techniques (see D12: page 856, "Cell Culture and Gene Expression") and (D15: page 959, "2.4: Cell culture and electrophysiology").

Finally, the issue at stake is whether the claimed subject-matter is sufficiently disclosed in view of whether the claimed therapeutic efficacy would have been credible on the basis of the information in the

application as filed and in light of common general knowledge. It is not relevant in this context whether the person skilled in the art would have been enabled to exactly reproduce an experiment mentioned only in the description to yield precisely the same data points. Neither claim 1 nor the dependent claims include any parametric feature (such as EC_{50}) or other requirement of this experiment.

4.5.3 Regarding point (c)

The test results presented in the form of a graph in Figure 7 of the application as filed show the concentration-dependent activity of p-anisaldehyde as an agonist of both hTRPA1 and hTRPV1, whereas no activation on hTRPM8 was observed. The asserted discrepancy between the EC_{50} value for TRPA1 activation mentioned in the description and the EC_{50} value as approximately derivable from the logarithmic concentration scale in Figure 7 does not call the observed effect as such into question.

Moreover, as established in point 4.5.5 below, the effect that is decisive for proof of concept is, in any case, the activation of TRPV1 rather than of TRPA1.

4.5.4 Regarding point (d)

D3 is a post-published document on a study that investigated the effects of several commercially available compounds found in indigenous Korean Mint (*Agastache rugosa*) on cultured hTRPA1- and hTRPV1-expressing cells (see D3: "Abstract"). p-anisaldehyde was one of the tested compounds.

D3 reports that p-anisaldehyde (1 mM) activated hTRPA1 but not hTRPV1 (see page 5: "Results", second to last paragraph).

As stated in D3 (see page 2, second to last paragraph and page 5: "Results"), the efficacy of a compound was determined by Ca^{2+} imaging analysis that involved monitoring the changes in cytosolic Ca^{2+} influx in hTRPA1- and hTRPV1-expressing cells using the fluorescent dyes Fura-2 AM and Fluo-4 AM.

Thus, the results reported in D3 were not obtained by the same method as disclosed in the application as filed, which measured ATP response rather than Ca^{2+} response (see point 4.5.2 above). There is no evidence provided by the parties as to how these methods might differ in sensitivity. For this reason, the statement in D3 that p-anisaldehyde was not found, by Ca^{2+} imaging analysis, to activate hTRPV1 is not conclusive for raising serious doubt about the positive result reported in the application as filed, which was reached by a different methodology.

4.5.5 Regarding point (e)

The disclosure of document D3 confirms, in principle, that p-anisaldehyde activates TRPA1. However, the board agrees with the appellant that there is no evidence on file of a clear and accepted relationship, at the relevant date, between TRPA1 agonism and improved swallowing (see also point 6.10.1 below).

The situation is different with TRPV1 agonism. The appellant did not contest that it was common general knowledge that the swallowing reflex could be promoted by activation of the TRPV1 channel, including by chemical agonists such as capsaicin. As established above (see point 4.5.4), the disclosure of D3 is not conclusive in raising serious doubt about the TRPV1 agonism of p-anisaldehyde that was demonstrated in the application as filed. Hence, the *in vitro* data on TRPV1 agonism in the application as filed is considered

sufficient for proof of concept of the alleged therapeutic efficacy of p-anisaldehyde.

4.5.6 Regarding point (f)

Dose finding is considered a routine activity in pharmaceutical development. In substantiation of claims relating to a further medical use, it is usually not required of applicants/patent proprietors to provide evidence outlining the boundaries of a therapeutic window.

The appellant did not provide any specific reason for its concern that the minimum dosage of p-anisaldehyde required to elicit a therapeutic effect might be so high that the claimed composition would be too unpleasant or toxic for patients to consume.

In the case in hand, there is no reason for serious doubt. p-anisaldehyde is a component of essential oils that are present in various edible foods. Unlike capsaicin, which is described in the application as filed (see paragraph [0007]) as "a particularly pungent and toxic compound", p-anisaldehyde is not known to provoke particularly unpleasant sensory perceptions. According to the application as filed (see paragraph [0015]), p-anisaldehyde had been described as having sweet, powdery, vanilla creamy, spice anise, nutty, cherry-pit and almond-like nuances.

Without further substantiation, the appellant's concern that there might not be a viable therapeutic window for p-anisaldehyde remains speculative.

4.5.7 Regarding point (g)

The postulated mechanism of action is set out in the application as filed (see point 2.4 above). It was also commonly known that TRP agonists such as capsaicin are applied orally. The person skilled in the art would

thus have been aware that the treatment according to claim 1 would require oral administration in the broad sense of providing contact of the active agent with the somatosensory fibres in the oral cavity. There is no requirement for an applicant/patent proprietor to provide guidance for hypothetical embodiments (such as, in this case, other routes of administration) that would in any case be recognised by the person skilled in the art as being impracticable.

4.6 The appellant, furthermore, argued that putting the envisaged treatment of oral pharyngeal dysphagia into clinical practice on the basis of *in vitro* data only would place an undue burden on the person skilled in the art.

4.7 This argument does not succeed for the following reasons.

4.7.1 After favourable *in vitro* results, dose-ranging studies would be the logical next step.

4.7.2 The appellant failed to provide a reason for serious doubt, substantiated by verifiable facts, that, in the case in hand, dose finding would present an unusual burden going beyond the routine work of the person skilled in the art. The fact that the application as filed does not specify a dosage range is not sufficient as a basis for serious doubt.

4.7.3 Dose finding for a medical use is, as a rule, considered to be a routine matter for the person skilled in the art. In the case at hand, the treatment elicits an immediate response, and the swallow reflex is a parameter that is easy to observe. Accordingly, dose-ranging studies would not be expected to present much difficulty.

4.7.4 The formulation of p-anisaldehyde in a suitable dosage form, such as a beverage or lozenge, would also be a routine activity.

4.8 For these reasons, the subject-matter of auxiliary request 1 complies with the requirement of sufficiency of disclosure under Article 83 EPC.

5. Auxiliary request 1 - novelty
(Articles 52(1) and 54 EPC)

5.1 D1 relates to a therapeutic agent for treating or ameliorating dysphagia which contains a TRPV1 agonist, in particular a capsaicin compound, or other substance that stimulates the auricular branch of the vagus nerve and which is to be applied to the ear canal. The other suitable substances include TRPM8 and TRPA1 agonists, menthol being a preferred TRPM8 agonist (see translation D2: claims and paragraphs [0012] and [0014] to [0018]). Further active agents, which are not TRPM8 or TRPA1 agonists but may generically be called TRP channel agonists, may be peppermint oil, spearmint oil or eucalyptus oil (see D2: paragraph [0018]).
The appellant argued that this constituted novelty-destroying disclosure since these essential oils also contain p-anisaldehyde.

5.2 The appellant's objection of lack of novelty over D1 must fail because the disclosure of peppermint oil, spearmint oil or eucalyptus oil in D1 does not amount to disclosure of p-anisaldehyde in a therapeutically effective amount as an agent that treats oral pharyngeal dysphagia (see point 1.3 above). Moreover, the appellant failed to show that D1 (published after the filing date of the application from which the patent in suit derives) is even comprised in the state

of the art under Article 54(2) or (3) EPC (see also Rules 165 and 159 EPC) (see point IX. above).

5.3 D5 discloses meals for easy swallowing for ALS patients, as suggested by patients. D5 includes, *inter alia*, recipes containing vanilla ice cream (page 9: "Mocha Frappé"; pages 14 to 18: several milkshakes). The appellant argued that this was novelty-destroying disclosure since vanilla contained p-anisaldehyde.

5.4 This argument cannot succeed because it cannot be derived conclusively from D5, or common general knowledge, that p-anisaldehyde must be present in these compositions, let alone that it is the pharmacologically active agent, present in a therapeutically effective amount, that treats oral pharyngeal dysphagia (see point 1.3 above).

According to D5, its recipes provide meals that are easy to swallow, based on the practical experience of patients. This effect is not attributed in D5 to vanilla, let alone p-anisaldehyde, which is not even mentioned as a potential component of vanilla. Since the recipes use ice cream as an ingredient, the skilled person reading D5 would instead attribute the effect of improved swallowing to cold stimulation, commonly known to be a beneficial factor.

In any case, the presentation of the recipes in D5 does not permit the reader to infer a specific qualitative and quantitative composition for the component designated as "vanilla", its concentration or the concentrations of any of its potential constituents. Nor is any active agent that facilitates swallowing identified.

5.5 For these reasons, the subject-matter of claim 1 of auxiliary request 1 is novel over the cited disclosure of D1 and D5 (Article 54 EPC). Since the remaining claims 2 to 6 are dependent claims, their subject-matter is also novel.

6. Auxiliary request 1 - inventive step (Articles 52(1) and 56 EPC)

Patent in suit

6.1 According to the patent in suit (paragraph [0008]), the inventors found that p-anisaldehyde is an agonist of the cation channels TRPA1 and TRPV1. It is believed that activation of TRPA1 and TRPV1 is effective in provoking a swallowing reflex in dysphagic patients.

Starting point in the prior art

6.2 According to the appellant, document D7 or document D8 may be used as a starting point for the assessment of inventive step.

6.3 According to D7, menthol (which was shown *in vitro* to activate the TRPM8 channel) may improve the sensitivity of the swallowing reflex in elderly patients with dysphagia, resulting in the prevention of aspiration pneumonia (D7: "Introduction"; "Discussion": first paragraph and first sentence of second paragraph). The study described in D7 showed that menthol, administered in water, can indeed improve the swallowing reflex (see page 370: "Results"; page 371, first paragraph). The authors of D7 conclude that their data suggest that menthol stimulation as well as cold stimulation restores sensitivity to the triggering of the swallowing reflex in dysphagic patients. They suggest that the addition of menthol to liquids and food may stimulate the swallowing reflex and help

prevent aspiration pneumonia in the elderly with dysphagia and that the menthol might conveniently be administered in the form of lozenges (see D7: page 371, left column). D7 is exclusively about an investigation of menthol and does not disclose p-anisaldehyde.

6.4 D8 is a review article on the diagnosis and management of oropharyngeal dysphagia in the elderly. Among other subjects, D8 also discusses the pharmacology of the swallow response in older people and mentions that agonists of TRPV1, such as capsaicin and piperine, had been reported to improve swallowing. D8 does not mention p-anisaldehyde.

Objective technical problem and solution

6.5 The appellant argued, *inter alia*, that the alleged technical effect was not achieved across the claimed scope because claim 1 covered non-working embodiments of compositions that would not achieve the claimed therapeutic benefit, in particular the administration of trace amounts or very high amounts of p-anisaldehyde was not excluded.

6.6 This objection fails because the technical effect in question is expressed in the claim.

Claim 1 of auxiliary request 1 is drafted in the format according to Article 54(5) EPC, and the therapeutic use stated in the claim is considered a limiting technical feature (see point 1.3 above). Thus, the technical effect of treating oral pharyngeal dysphagia is by definition achieved across the claimed scope. In other words, non-working embodiments are not claimed.

The appellant's objection that not all conceivable compositions, or rather dosages, of p-anisaldehyde might achieve the stated therapeutic effect should, therefore, have been raised in the context of

sufficiency of disclosure rather than inventive step (see G 1/03, OJ EPO 2004, 413, Reasons: 2.5.2).

As established in point 4.5.6 and section 4.7 above, the absence of a specified dosage range in claim 1 does not lead to a finding of insufficiency of disclosure, and also the appellant's further arguments why the therapeutic effect was not credible across the entire scope or for part of the scope claimed were found unconvincing (see section 4.5). Also for this reason, it has to be acknowledged that the therapeutic effect is obtained across the claimed scope.

6.7 The claimed subject-matter differs from the disclosure of D7 and D8 by the identity of the active agent used, which is p-anisaldehyde instead of menthol (in D7) or capsaicin and piperine (in D8).

6.8 Since no comparative data in relation to the active agents of D7 and D8 is on file, the objective technical problem starting from either D7 or D8 can be defined as the provision of a composition with an alternative active agent for use to treat oral pharyngeal dysphagia.

Obviousness of the solution

6.9 The question to be answered is whether the person skilled in the art seeking to solve the objective technical problem would have found it obvious, having regard to the state of the art, to use compositions containing p-anisaldehyde as the active agent that treats dysphagia.

6.10 This question has to be answered in the negative for the following reasons.

6.10.1 None of the cited prior-art documents disclose or suggest that p-anisaldehyde has the effect of helping

with the swallowing process or that it is a TRP agonist providing the same therapeutic effect as the TRPM8 and TRPV1 agonists discussed in D7 and D8.

The prior art on file does not disclose that

- TRPA1 stimulation is a relevant mechanism
- p-anisaldehyde is an agonist of TRPA1
- p-anisaldehyde is an agonist of TRPV1

As to the first of these aspects, D7, in its closing paragraphs, mentions in passing that further studies were needed to elucidate the possible involvement of TRPA1 in the swallowing reflex (see D7: page 371, left column, second paragraph) and that TRPA1 is stimulated by cinnamaldehyde and mustard oil, but not by menthol.

In its section "7. Future perspectives", D14 references an earlier study that purportedly suggested that TRPA1 agonists such as allyl isothiocyanate and cinnamaldehyde may be beneficial for the swallowing reflex but concludes that further research is needed to uncover the effects of these agonists (see D14: page 103, left column).

Neither statement amounts to unambiguous disclosure of TRPA1 agonism as an established mechanism for improved swallowing, and neither document mentions p-anisaldehyde.

6.10.2 In its written submissions, the appellant cited D2, D3 and D4 as supplementary documents to be combined with the teaching of D7, and D3, D4, D9, D10 and D11 as supplementary documents to be combined with the teaching of D8.

- D2 is merely a translation of D1 into English. As mentioned above (see points IX. and 5.2), the appellant failed to demonstrate that D1 is part of the state of the art under Article 54(2) EPC.

Hence, D1 cannot be taken into account for the assessment of inventive step. D1 would in any case have been irrelevant as it does not contain any teaching on p-anisaldehyde and its pharmacological effects (see point 5.1 above).

- Because D3 was published after the filing date of European patent application No. 14739842.4, from which the patent in suit derives, it is not part of the state of the art that can be taken into account in the assessment of inventive step.

- D4 discloses that Yakima double-cut peppermint oil (*Mentha piperita L.*) comprises p-anisaldehyde as one of 177 components listed in Table 2 of D4. This is the only mention of p-anisaldehyde in D4. There is no teaching about any specific pharmacological activity of p-anisaldehyde or its impact on the swallowing reflex. Starting from the teaching in D7 about menthol or from the teaching in D8 about capsaicin, the person skilled in the art would not have consulted the unrelated D4, which is a chemical analysis of peppermint oil. There is also no reason why the person skilled in the art should have expected components of peppermint oil that are chemically different from menthol to have the same activity as menthol.

- D9 (paragraph 4.3.2) discloses that herbal cough remedies may contain essential oils such as, *inter alia*, peppermint oil, anise oil or eucalyptus oil. These produce a pleasing taste sensation that stimulates the secretion of saliva, which in turn activates the swallowing reflex. Starting from the teaching in D7 about menthol or from the teaching in D8 about capsaicin, the person skilled in the art would not have consulted the entirely unrelated document D9 on herbal cough remedies. There is also

no teaching in D9 about p-anisaldehyde and its properties or activity. The mere observation in D9 that the administration of essential oils may indirectly increase the secretion of saliva cannot be conclusive in this regard.

- D10 discloses that the essential oil of aniseed (*Pimpinella anisum*) contains p-anisaldehyde. D10 mentions various properties of aniseed oil and its main components but does not teach that p-anisaldehyde may stimulate swallowing.
- D11 is a post-published document that, like D3, cannot be taken into account in the assessment of inventive step.

Thus, none of the supplementary documents cited by the appellant is relevant to the issue in hand.

6.10.3 In conclusion, p-anisaldehyde was not disclosed or suggested by the prior art as a potential alternative therapeutic agent to menthol, capsaicin or piperine for treating oral pharyngeal dysphagia.

6.11 As a consequence, the subject-matter of claim 1 of auxiliary request 1 involves an inventive step within the meaning of Article 56 EPC. The subject-matter of dependent claims 2 to 6 also involves an inventive step for the same reasons.

7. Conclusion

In the absence of other objections, the set of claims of auxiliary request 1 is found allowable.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent in amended form on the basis of claims 1 to 6 of the new auxiliary request 1 submitted at the oral proceedings before the board, and, if appropriate, a description and drawings adapted thereto.

The Registrar: The Chairwoman:

I. Aperribay M. Pregetter

Decision electronically authenticated