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Datasheet for the decision of 29 April 2024

Case Number: T 1863/21 - 3.3.09

Application Number: 11723272.8

Publication Number: 2575508

IPC: A23L33/17, A23L33/21

Language of the proceedings: EN

Title of invention:
NON-DIGESTIBLE OLIGOSACCHARIDES FOR ORAL INDUCTION OF TOLERANCE AGAINST DIETARY PROTEINS

Patent Proprietor:
N.V. Nutricia

Opponent:
Société des Produits Nestlé S.A.

Headword:
Enhancement of oral tolerance/NUTRICIA

Relevant legal provisions:
EPC Art. 56, 100(b)
RPBA 2020 Art. 12(6)

Keyword:

Late-filed evidence - error in use of discretion at first instance (no)
Claim construction - mechanism of action
Sufficiency of disclosure - (yes) - after amendment
Inventive step - (yes)

Decisions cited:

G 0006/88, G 0002/08, T 0254/93, T 0486/01, T 1020/03, T 0884/06, T 1972/14, T 0299/18, T 1776/18, T 2036/21

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Case Number: T 1863/21 - 3.3.09

D E C I S I O N
of Technical Board of Appeal 3.3.09
of 29 April 2024

Appellant: (Opponent)	Société des Produits Nestlé S.A. Avenue Nestlé 55 1800 Vevey (CH)
Representative:	Plougmann Vingtoft a/s Strandvejen 70 2900 Hellerup (DK)
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Representative:	Nederlandsch Octrooibureau P.O. Box 29720 2502 LS The Hague (NL)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 15 July 2021 rejecting the opposition filed against European patent No. 2575508 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	A. Haderlein
Members:	F. Rinaldi
	N. Obrovski

Summary of Facts and Submissions

I. This decision concerns the appeal filed by the opponent (appellant) against the opposition division's decision to reject the opposition against the European patent.

II. In the notice of opposition, the opponent had requested that the patent be revoked under Article 100(a) (lack of inventive step) and 100(b) EPC.

III. The following documents are referred to in this decision:

D1: J. Beaulieu *et al.*, "Whey proteins and peptides: beneficial effects on immune health", Therapy, 3(1), 2006, 69-78

D2: S. Pecquet *et al.*, "Peptides obtained by tryptic hydrolysis of bovine β-lactoglobulin induce specific oral tolerance in mice", Journal of Allergy and Clinical Immunology, 105(3), 2000, 514-521

D3: R. Fritsché *et al.*, "Induction of systemic immunologic tolerance to β-lactoglobulin by oral administration of a whey protein hydrolysate", Journal of Allergy and Clinical Immunology, 100(2), 1997, 266-273

D4: EP 0 629 350 A1

D8: D. Charalampopoulos *et al.*, "Prebiotics and Probiotics Science and Technology", New York: Springer Science+Business Media, 2009, 903

D10: G. Boehm *et al.*, "Structural and Functional Aspects of Prebiotics Used in Infant Nutrition", The Journal of Nutrition, 138, 2008, S1818-S1828

D11: B. Schouten *et al.*, "Oligosaccharide-Induced Whey-Specific CD25 Regulatory T-Cells Are Involved in the Suppression of Cow Milk Allergy in Mice", The Journal of Nutrition, 140(4), 2010, 835-841

D13: F. Savino *et al.*, "Reduction of crying episodes owing to infantile colic: a randomized controlled study on the efficacy of a new infant formula", European Journal of Clinical Nutrition, 60, 2006, 1304-1310

D15: Additional experimental data (filed by the patent proprietor by letter dated 18 February 2020)

D15a: Unpaired t-test results (filed by the opponent by letter dated 27 June 2021)

D21: V. Amrhein *et al.*, "Retire statistical significance", Nature, 567, 2019, 305-307

IV. On appeal, the patent proprietor (respondent) maintained the auxiliary requests it had filed during the opposition proceedings, namely auxiliary requests 1 to 11 (originally filed by letter dated 18 February 2020) and 1a to 11a and 1b (originally filed by letter dated 24 September 2020).

V. Wording of the claims relevant to the decision

Relevant to this decision are claims 1 and 2 of the patent as granted (main request). They read as follows.

"*1. At least one non-digestible oligosaccharide selected from the group consisting of fructo-oligosaccharide, non-digestible dextrin, galacto-oligosaccharide, xylooligosaccharide, arabino-oligosaccharide, arabinogalacto-oligosaccharide, gluco-oligosaccharide, glucomanno-oligosaccharide,*

galactomannooligo-saccharide, mannan-oligosaccharide, chito-oligosaccharide, uronic acid oligosaccharide, sialyloligosaccharide and fuco-oligosaccharide for use in the enhancement of a partial protein hydrolysate-induced oral tolerance against dietary proteins, the partial protein hydrolysate being characterised in that it comprises at least 3 wt% of peptides with a size of 5 kDa or above and at least 50 wt.% of peptides with a size below 5 kDa and wherein the partial protein hydrolysate is partial mammalian milk protein hydrolysate, partial whey protein hydrolysate or partial beta-lactoglobulin hydrolysate."

"*2. Enteral composition comprising at least one non-digestible oligosaccharide selected from the group consisting of fructo-oligosaccharide, non-digestible dextrin, galacto-oligosaccharide, xylo-oligosaccharide, arabino-oligosaccharide, arabinogalacto-oligosaccharide, gluco-oligosaccharide, glucomannooligo-saccharide, galactomanno-oligosaccharide, mannan-oligosaccharide, chitooligosaccharide, uronic acid oligosaccharide, sialyloligosaccharide and fucooligosaccharide and at least one partial protein hydrolysate, for use in the induction of oral tolerance against cow's milk protein, wherein the at least one non-digestible oligosaccharide enhances partial protein hydrolysate-induced oral tolerance, the partial protein hydrolysate being characterized in that it comprises at least 3 wt.% of peptides with a size of 5 kDa or above and at least 50 wt.% of peptides with a size below 5 kDa and wherein the partial protein hydrolysate is partial mammalian milk protein hydrolysate, partial whey protein hydrolysate or partial beta-lactoglobulin hydrolysate.*"

Claim 1 of auxiliary requests 1 to 5, 1a to 5a and 1b includes additional features which restrict the claim. Nevertheless, the first claims of all these requests encompass the feature "*against dietary proteins".*

Claim 1 of auxiliary request 6 is based on claim 1 of the patent as granted, the only difference being that the feature "*against dietary proteins*" reads "*against milk proteins*".

VI. The appellant's arguments relevant to this decision can be summarised as follows:

- The opposition division erred in not admitting document D15a into the proceedings. This document had to be admitted on appeal.
- Claims 1 and 2 had to be interpreted as being directed to compositions comprising a mixture of a partial protein hydrolysate and non-digestible oligosaccharides, the mixture exhibiting enhanced induction of oral tolerance.
- If not, the invention was not sufficiently disclosed. There was no credible evidence that enhanced induction of oral tolerance had to be attributed to the non-digestible oligosaccharides. A statistical analysis of the data of D15 showed that a blend of galacto-oligosaccharides and fructo-oligosaccharides did not enhance partial protein hydrolysate-induced oral tolerance. Moreover, claims 1 and 2 were not restricted to the administration regimen shown in the patent. Finally, claim 1 aimed at achieving oral tolerance against any type of dietary protein. This result could not be achieved with just the milk protein hydrolysates of claim 1.

- The subject-matter of claims 1 and 2 lacked inventive step starting from D4 as the closest prior art in combination with D11.

VII. The respondent argued as follows:

- The opposition division had correctly decided not to admit D15a into the proceedings.
- Claims 1 and 2 had to be construed as being restricted to the oligosaccharides for use in enhancement of partial protein hydrolysate-induced oral tolerance against dietary proteins.
- Examples 1, 3 and 4 of the patent and D15 demonstrated that the effect described in the patent and called for in claims 1 and 2 was achieved. Therefore, the invention was sufficiently disclosed.
- The subject-matter of claim 1 involved an inventive step starting from D4 as the closest prior art. None of the cited prior-art documents taught the use of non-digestible oligosaccharides to enhance partial protein hydrolysate-induced oral tolerance.

VIII. Final requests

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 (main request) or, alternatively, that the patent be maintained in amended form according to one of auxiliary requests 1 to 11 filed by letter of 18 February 2020, or according to one of auxiliary requests 1a to 11a or 1b filed by letter of 24 September 2020.

Reasons for the Decision

1. *Admittance of D15a*

1.1 The opponent filed document D15a with the EPO on a Sunday, two days before the oral proceedings before the opposition division. In D15a, the data in D15 were statistically analysed. D15 concerns experimental data filed by the patent proprietor under Rule 79(1) EPC, in reply to the opponent's notice of opposition. The analysis in D15a allegedly demonstrated that the data were not statistically significant.

1.2 The opposition division decided not to admit D15a. The reasoning for its decision was as follows:

- The arguments and conclusions given in D15a had been presented earlier, within the final date set in accordance with Rule 116(1) EPC.
- D15a itself was submitted only two days prior to the date of the oral proceedings. This prevented the patent proprietor from verifying the calculations.
- Since the calculations were no more relevant than the arguments already presented, the document was not admitted into the proceedings.

1.3 When reviewing the discretionary decision of an opposition division on a procedural matter, a board normally maintains this decision if the opposition division has exercised its discretion firstly according to the right principle(s) and secondly in a reasonable way.

1.4 The end of the opposition period under Article 99(1) EPC is a fixed point in time, as of which an opposition division has discretion not to admit facts and evidence submitted by an opponent (see T 1776/18, point 4.6.4 of the Reasons, with further references). As to the opposition division's exercise of discretion, the board notes, first and foremost, that while D15 was provided at the earliest point in time in the opposition proceedings, the same cannot be said of D15a. Filing D15a only two days before the oral proceedings before the opposition division meant that not only the patent proprietor (and its experts, if available) but also the opposition division had to deal with the new calculations at very short notice.

1.5 The opposition division was correct in relying on the criterion of *prima facie* relevance when deciding on the admittance of D15a and did not commit any error when assessing the document according to this standard. At the oral proceedings, the opposition division considered the data in D15a to be no more relevant than the arguments and conclusions it was already aware of. This assessment is straightforward and conclusive. Thus, the board cannot identify any error in the opposition division's discretionary decision not to admit D15a.

1.6 It is noted for completeness, that the appellant itself did not refer to D15a during the oral proceedings before the board.

1.7 To conclude, there is no reason to admit this document on appeal (Article 12(6) RPBA).

2. *Claim interpretation*

2.1 A main issue of dispute between the parties was how claims 1 and 2 of the patent as granted (main request) are to be read and construed.

2.1.1 For the appellant, claim 1 and in particular claim 2 as granted were directed to compositions comprising a mixture of a partial protein hydrolysate and non-digestible oligosaccharide that induced oral tolerance to proteins. The feature of enhancement in claims 1 and 2 meant that the mixture exhibited induction of oral tolerance that was enhanced compared to that achieved by a composition with partial protein hydrolysate only. In other words, the enhancement was implicit to the co-administration of at least one non-digestible oligosaccharide and the specified partial protein hydrolysates for inducing oral tolerance. Put differently, claims 1 and 2 were directed to a mechanism of action and according to established case law such a feature had to be ignored when construing the claims.

2.1.2 The opposition division and the respondent interpret claims 1 and 2 as granted in a different way. Their interpretation does not focus on the aspect that a mixture is used (as is implicit from claim 1 as granted and explicitly required by claim 2 as granted) but rather on the role of the non-digestible oligosaccharide. The role consists in enhancing the oral tolerance induced by the specified partial protein hydrolysates.

2.2 To address the issue of how to construe the claims, it is necessary to look more closely at the wording used in them.

2.2.1 In a simplified form, claim 1 of the patent as granted is directed to a non-digestible oligosaccharide for use in the enhancement of oral tolerance against dietary proteins, the oral tolerance being induced by specified partial protein hydrolysates.

2.2.2 In a similarly simplified form, claim 2 of the patent as granted is directed to a composition comprising a non-digestible oligosaccharide and a specified partial protein hydrolysate, for use in the induction of oral tolerance against cow's milk protein. The non-digestible oligosaccharide enhances the oral tolerance induced by the partial protein hydrolysate.

2.2.3 Needless to say, the primary aim of the wording used in a claim is to define the matter for which protection is sought in terms of the technical features of the invention, having regard to the particular nature of the subject invention and to the purpose of such claims (G 6/88, Reasons 2.5).

2.3 It is common ground between the parties to the proceedings that claims 1 and 2 as granted are medical use claims. The board agrees. The medical use of these claims consists in inducing oral tolerance against proteins. The feature of enhancement is considered a functional feature within the specific medical use of claims 1 and 2.

2.4 In more detail, claims 1 and 2 as granted require the use of specific partially hydrolysed proteins (i.e. protein fragments) which induce oral tolerance. This is

a mandatory feature of the two claims. Within this specific use, the claims also define the role of the non-digestible oligosaccharide, which is to exhibit the effect of enhancing the oral tolerance-inducing effect of the partially hydrolysed proteins. This is what a plain, straightforward reading of claims 1 and 2 would disclose to the skilled person. Needless to say, spelling out this role further restricts the scope of these claims: it is mandatory that the enhancement is due to the non-digestible oligosaccharide, while the partial protein hydrolysate is responsible for oral tolerance.

2.5 This interpretation is also supported by the patent specification and the examples disclosed in it. Enhancement by non-digestible oligosaccharides is a major aspect disclosed throughout the patent, above all in the section of the detailed description of the invention in paragraphs [0022] to [0037]. Examples 1, 3 and 4 show that non-digestible oligosaccharides alone have next to no effect on the induction of oral tolerance, whereas partial protein hydrolysates do have such an effect. Furthermore, the effect of the partial protein hydrolysate is increased if it is administered in association with at least one non-digestible oligosaccharide.

2.6 The experimental set-up chosen for and disclosed in the patent is suitable for demonstrating that the at least one non-digestible oligosaccharide enhances the oral tolerance induced by specific partial protein hydrolysates. While other conclusions might be drawn from the results in the patent's examples, the results themselves clearly support (and certainly do not contradict) the fact that enhancement occurs. To what extent the experiments are sufficient to demonstrate

that the invention is enabled (and moreover over the entire scope) will be discussed below, in section 3 of this decision.

2.7 The question remains as to whether the feature of enhancement, construed as set out above, merely sets out a mechanism of action. The appellant's contention was that a feature relating to such a mechanism had to be ignored. In this context it referred to T 1972/14. According to this decision, a (second) medical use claim "can derive novelty from the claimed therapeutic effect, but not from the mechanism underlying it" (Reasons, 1.1).

2.8 This line of argument is not convincing.

2.8.1 It is uncontested that the subject-matter of medical use claims 1 and 2 under scrutiny is novel. There is no prior art disclosing at least one non-digestible oligosaccharide (selected from the lists in claims 1 and 2) and the specified partial protein hydrolysate which induces oral tolerance.

2.8.2 To the best of this board's knowledge, aspects relating to a mechanism of action have been discussed in decisions of the Boards of Appeal only in cases where such a mechanism was the only distinguishing feature over the prior art. The appellant itself did not point to any decision of the Boards of Appeal in which an alleged mechanism of action in a medical use claim was discussed for purposes other than for establishing novelty of the subject-matter claimed (as was done for instance in T 1972/14, T 254/93 and T 486/01).

2.8.3 What is more, contrary to the appellant's allegation, a reference to a mechanism of action may even lead to

novel subject-matter, provided that it leads to a truly new useful application arising from e.g. the opening of a new field of clinical application (T 1020/03, Reasons 42; G 2/08, Reasons 5.10.7).

2.8.4 In fact, these two decisions indicate that there is no particular restriction on how an applicant (or patent proprietor) formulates a medical use claim, as long as its subject-matter results in a therapy that is novel and inventive (T 1020/03, Reasons 48; G 2/08, Reasons 5.10.9). The applicant (or patent proprietor) therefore has a certain degree of freedom in how it drafts a claim and what (limiting) features it chooses to include in the wording of the claim.

2.8.5 Therefore, the (academic) question as to whether the feature of enhancement relates to a mechanism of action has in itself no bearing on how the medical use claims under scrutiny are construed. The important aspect is that the feature of enhancement restricts the scope of claims 1 and 2.

2.9 To conclude, claims 1 and 2 specify, and at the same time require, that enhancement is due to the non-digestible oligosaccharide and that the partial protein hydrolysate is responsible for inducing oral tolerance. This interpretation of claims 1 and 2 will be used for examining the contested patent.

2.10 For completeness, the board notes that it follows from this claim interpretation that a simple mixture of at least one non-digestible oligosaccharide and the specified partial protein hydrolysates for inducing oral tolerance - in which the role of the oligosaccharide is not identified - would not anticipate the subject-matter of claims 1 and 2 as

granted. The reason for this is that such a simple mixture would not disclose the aforementioned functional features of claims 1 and 2 as granted. Instead, these two claims are restricted to a specific medical use that involves applying the at least one non-digestible oligosaccharide for enhancing the effect of the specific partial protein hydrolysate.

3. *Ground for opposition under Article 100(b) EPC*

3.1 The appellant contested the opposition division's decision that the invention was sufficiently disclosed. It argued as follows:

- There was no evidence that allowed the conclusion to be drawn that non-digestible oligosaccharide enhanced the partial protein hydrolysate's ability to induce oral tolerance over the entire scope. A statistical analysis of the data in D15 showed that a blend of galacto-oligosaccharides and fructo-oligosaccharides did not enhance partial protein hydrolysate-induced oral tolerance.

- D11 showed that, depending on the administration pattern, a specific blend of non-digestible oligosaccharides alone induced oral tolerance to whey proteins. Therefore, non-digestible oligosaccharide contributed to the induction of oral tolerance. It followed from this that the claims were not restricted to what caused the enhancement within the narrow meaning of the patent.

- Claim 1 was directed to induction of oral tolerance against dietary protein; however, it was not possible to achieve this effect for all dietary

proteins when only milk protein hydrolysates were used.

3.2 For assessing sufficiency of disclosure, the patent's examples are particularly relevant, starting with example 1.

3.2.1 This example relates to several sets of experiments carried out on mice. The results are shown on table 2. The pre-treatment consisted in orally administering to the different groups of mice the components to be investigated. One group of mice received no pre-treatment (control group). The pre-treatment was stopped, and after two days the mice were repeatedly sensitised orally with whey protein, using a blunt needle. As a final step, the mice were challenged intradermally with whey protein near their ears. The allergic response was measured by the thickness of the ear swelling. The following three components (among others) were tested in the pre-treatments which the different groups of mice underwent:

- a partially hydrolysed whey protein ("pWH")
- a blend of three non-digestible oligosaccharides ("NDO")
- a partially hydrolysed whey protein and a blend of three non-digestible oligosaccharides ("pWH + NDO")

3.2.2 The mice receiving the partially hydrolysed whey protein ("pWH" group) showed a reduced acute ear-swelling response after intradermal whey protein challenge. Pre-treatment with a non-digestible oligosaccharide mixture ("NDO" group) led to significant ear swelling, similar to that observed in the group of mice that received no pre-treatment (control group). The strongest effect in terms of

reducing ear swelling was observed in mice pre-treated with both partially hydrolysed whey protein and non-digestible oligosaccharides ("pWH + NDO" group).

3.2.3 The test set-up chosen in example 1 is suitable for demonstrating the enhancing role of non-digestible oligosaccharides. This applies in particular to the aspect of administering the non-digestible oligosaccharides only during the pre-treatment phase and not during the sensitisation phase. The appellant did not argue that the set-up would have been unsuitable for showing enhancement, let alone that there was any better way of demonstrating enhancement.

3.2.4 Summing up the experimental results shown in example 1, in view of

- the good results for the "pWH" group
- the improved effect for the "pWH + NDO" group
- the next to no effect for the "NDO" group

the conclusion that has inevitably to be drawn is that non-digestible oligosaccharides enhance the partial protein hydrolysate's ability to induce oral tolerance.

3.2.5 Analogous results are shown also in examples 3 and 4 of the patent. These confirm the findings in example 1.

3.2.6 It is correct that the experiments in the patent's examples were carried out with a ternary blend of non-digestible oligosaccharides (trans-galacto-oligosaccharides, long chain fructo-oligosaccharides and galacturonic acid oligosaccharides). But in the current case, the board sees no indication that the concept of enhancing the oral tolerance induced by

partial protein hydrolysate will not work if different non-digestible oligosaccharides are used.

3.3 Considering all this, the invention as disclosed in the patent can be accepted as sufficiently disclosed.

3.4 To support the argument that the invention was sufficiently disclosed over the whole scope, the patent proprietor even filed further experimental tests (D15) with its reply to the notice of opposition.

3.4.1 D15 discloses experiments carried out with a set-up similar to that of example 1 of the patent. The main difference is that in D15 a binary blend of non-digestible oligosaccharides (trans-galacto-oligosaccharides and fructo-oligosaccharides) is used to enhance the effect of the partial protein hydrolysate, as opposed to the ternary blend used in example 1.

3.4.2 The results in terms of ear swelling in the mice subjected to the tests are plotted (group by group) in the sole figure of D15. The figure shows the individual swelling of the ear measured for each mouse in each treated group.

3.4.3 On the face of it, the results in the figure of D15 confirm the results of example 1 of the patent. A visual inspection of the figure with the naked eye shows that the ear swelling is slightly less in the group of mice receiving the combination of partially hydrolysed whey protein with the binary mixture of non-digestible oligosaccharides ("GF" group). The group of mice receiving partially hydrolysed whey protein alone ("pWH" group) has a slightly more pronounced ear swelling. This is confirmed by comparing the mean

values for ear swelling calculated for each of the two groups.

3.5 The appellant did not criticise the test set-up used in the patent. It even conceded that the results in the patent's examples for the ternary blend of non-digestible oligosaccharides may show an effect. However, the appellant disputed that such an effect was achieved when only one or two non-digestible oligosaccharides were used. In other words, the allegation was that the result was not achieved over the entire scope of claims 1 and 2.

3.6 The appellant did not provide its own experimental data in order to argue this point. Instead, its only line of argument on this aspect was based on a statistical analysis of the results shown in the figure of D15.

3.7 In more detail, the appellant:

- magnified the figure of D15
- measured the ear-swelling values for the various data points from the magnified figure
- subjected the values for the data points to a statistical analysis
- identified an outlier in the values measured, i.e. it assessed that it was highly unlikely that the identified outlier data point was a true member of the data set
- stated that it was mandatory to apply basic scientific principles established in statistics according to which data points identified as outliers had to be excluded
- explained that, based on its calculations, the mean value obtained for the "GF" group and the

"pWH" group were similar and no statistically relevant results could be drawn from these results

- concluded that the invention was not sufficiently disclosed, at least when a binary composition of oligosaccharides was used

3.8 However, statistical significance is not and should not be the sole criterion for considering experimental results, let alone for excluding them from consideration. In T 884/06, the entrusted board concluded that the effect under scrutiny was demonstrated "even though the actual statistical significance might be arguable" (Reasons 17). This board, in a different composition, decided in T 299/18 (Reasons 3.6.7) that the data in the contested patent underlying that decision did not necessarily have to "show a statistically significant difference that stands up to strict, mathematical scrutiny of the data". After all, a patent need not fulfil the standards that a peer-reviewed scientific publication might have to comply with.

3.9 Indeed, this board subscribes to the view expressed in the Catchword of T 2036/21, by this board in a different composition, that the principle of the free evaluation of evidence applies universally in proceedings before the EPO when assessing any means of evidence. The deciding body decides in the light of its own conviction, taking into account the evidence available in the proceedings and on the footing that one set of facts is more likely to be true than the other. In proceedings before the EPO, it is thus not a prerequisite to perform a statistical analysis of the results and to determine a specific confidence interval in order to consider a certain piece of evidence convincing, as it is most often required in biomedical

research and by health authorities granting marketing authorisations for medicinal products.

3.10 Statistical significance quantifies the probability that an observed difference in data is not a random occurrence. Hence, the allegation of lack of statistical significance does not in itself prove the null hypothesis, i.e. the hypothesis that there is no difference between groups, or no effect of a treatment. This is explained in detail in D21, a document that discusses the relevance of statistical significance when reporting on crucial effects in scientific publications.

3.11 Therefore, lack of statistical significance does not automatically render a demonstrated effect implausible for the purposes of a legal assessment. Similarly, classifying a data point as an outlier is simply a statement on the probability that the data point is not a true member of the data set. In the current case, this in itself is not sufficient to set aside and disregard the remaining results.

3.12 Even if one were to follow the appellant's conclusion that the results in D15 were indeed not statistically relevant, such a conclusion would not be decisive in changing the board's assessment on sufficiency of disclosure. The appellant would have had to raise serious doubt that the invention is not sufficiently disclosed over the entire scope. Under the circumstances of the present case, and in view of the patent's examples, the appellant's finding on the statistical relevance of the data in D15 is not sufficient to raise doubt that can be qualified as serious.

3.13 The appellant also argued that D11 showed that non-digestible oligosaccharides were able to induce oral tolerance against milk proteins. In D11, the oligosaccharides were administered to mice throughout the entire experiment and not only in the pre-treatment phase, as in the patent's examples. Therefore, in D11 the total amount of oligosaccharides administered in D11 was much higher than in the patent in suit. The appellant concluded from this analysis that the invention defined in the claims was not restricted to the dosage regimen (i.e. a pre-treatment) that provided the enhancement. In its view, failure to mention the pre-treatment rendered the invention insufficiently disclosed over the entire scope covered by the claims.

3.14 However, as explained above, the experiments in the patent show that the at least one non-digestible oligosaccharide provides enhancement of the oral tolerance obtained by the specific partial protein hydrolysate. Moreover, claims 1 and 2 of the patent as granted are restricted to enhancement. Therefore, no reason can be seen why a further restriction of the claims would have to be added: the wording of claims 1 and 2 already restricts the claims to the use that involves enhancement.

3.15 The appellant also argued that the patent disclosed that synergistic enhancement was achieved. The appellant contested that every embodiment covered by the claims of the patent as granted achieved such a synergistic effect.

3.16 However, claims 1 and 2 aim solely at achieving enhancement of the action of the specific partial protein hydrolysate. The enhancement need not be synergistic over the entire scope of claims 1 and 2. As

explained above, the board is satisfied that an enhancement is demonstrated. Furthermore, the patent shows also how an enhancement can be provided that can be assessed as being synergistic. For instance, this may be achieved using the non-digestible oligosaccharide blend used in example 1.

3.17 The appellant finally disputed that the invention set out in claim 1 was sufficiently disclosed over the entire scope. The claim referred to oral tolerance against dietary proteins but the protein fragments defined in the claim could only generate oral tolerance against milk proteins. This followed directly from the principle according to which protein epitopes developed immunological tolerance. As even the respondent admitted, the identity of the partial protein hydrolysates determined the intact dietary proteins to which immunological tolerance was developed.

3.18 As to this specific objection, it is straightforwardly clear that the partial protein hydrolysates to which claim 1 is restricted are not suitable for inducing oral tolerance against any dietary protein. The partial milk protein hydrolysates of claims 1 and 2 provide oral tolerance only to the corresponding intact protein, i.e. milk protein. This is discussed in the prior art on the development of oral tolerance with protein hydrolysate and peptides from milk, for example in D1, D2, D3 and D4 cited in these proceedings.

3.19 In this respect it is manifest that claim 1 is not sufficiently disclosed over the entire scope that it covers and for which protection is sought. Therefore, in view of this specific objection (lack of sufficient disclosure over the entire scope claimed in view of the dietary protein), and only this specific objection, the

board concludes that the invention is not sufficiently disclosed.

3.20 Therefore, in view of the fact that claim 1 refers to dietary proteins, the ground for opposition under Article 100(b) EPC prejudices maintenance of the patent as granted.

4. *Auxiliary request 1 to 5, 1a to 5a and 1b*

4.1 The first claim of all requests ranking higher than auxiliary request 6 requires oral tolerance to be achieved against dietary proteins. These requests are auxiliary requests 1 to 5 filed by letter dated 18 February 2020 and auxiliary requests 1a to 5a and 1b filed by letter dated 24 September 2020.

4.2 In this respect, the same objection of lack of sufficiency of disclosure valid for claim 1 of the patent as granted applies to auxiliary requests 1 to 5 filed by letter dated 18 February 2020 and to auxiliary requests 1a to 5a and 1b filed by letter dated 24 September 2020.

5. *Auxiliary request 6*

5.1 Conversely, claim 1 of auxiliary request 6 filed by letter dated 18 February 2020 is restricted to oral tolerance against milk proteins. The board is satisfied that this amendment resolves the only successful objection of lack of sufficiency of disclosure against the claims as granted.

5.2 The only remaining issue to decide is inventive step for claims 1 and 2 of this request. In the decision under appeal, the opposition division decided that the

subject-matter of claims 1 and 2 as granted involved an inventive step.

5.3 On appeal, the parties agreed that D4 was the closest prior art and that the distinguishing features were those identified by the opposition division, namely that D4 does not disclose:

(i) partial whey protein hydrolysates that contain non-digestible oligosaccharides

(ii) that non-digestible oligosaccharides, if combined with a partial whey protein hydrolysate, enhance the induced oral tolerance

5.4 The board has no reason to differ.

5.5 Furthermore, the appellant agreed that the technical problem may be formulated in the terms used by the opposition division. Therefore, the problem to be considered for assessing inventive step of claims 1 and 2 is how to improve partial protein hydrolysate-induced oral tolerance to milk proteins.

5.6 The contentious point was essentially whether the solution would have been obvious to the skilled person.

5.6.1 According to the appellant, the skilled person would have immediately realised that enhancement could only be achieved by adding a further substance. They would then have arrived at D11, which is concerned with induction of oral tolerance, and learned from the document about the role of non-digestible oligosaccharides. Finally, they would have used the ternary blend of non-digestible oligosaccharides described in D11 to solve the problem.

5.6.2 This line of argument fails to convince the board. The closest prior art teaches specific partial protein hydrolysates for inducing oral tolerance. It is not conclusive why the skilled person would arrive at a document that does not rely on, let alone mention, protein fragments for inducing oral tolerance.

5.6.3 Indeed, D11 relates to a different mechanism for addressing oral tolerance. In particular, it does not address how to improve partial protein hydrolysate-induced oral tolerance to dietary proteins or cow's milk protein. As the appellant acknowledged, D11 "solves the problem of enhancing oral tolerance in a way that is completely independent of the protein source" (statement setting out the grounds of appeal, page 29, underlining in the original). Therefore, there is nothing that would have prompted the skilled person to turn to D11 and the non-digestible oligosaccharides disclosed in it to solve the problem.

5.6.4 Even if the skilled person were to combine the teaching of D4 and D11, they would not have arrived at the combination of features of claims 1 and 2. In particular, they would not have envisaged the enhancement of oral tolerance induced by the partial protein hydrolysate that is achieved by the at least one non-digestible oligosaccharide.

5.6.5 In a secondary line of argument, the appellant also referred to D8, D10 and D13. These documents discussed beneficial effects of non-digestible oligosaccharides in the context of food allergies. However, none of these documents deals with inducing oral tolerance, let alone how to enhance it. Therefore, without the benefit

of hindsight, the skilled person would not have consulted these documents.

5.6.6 To conclude, the solution provided in claims 1 and 2 would not have been obvious to the skilled person starting from the teaching of D4.

5.7 The provisions of Article 56 EPC do not prejudice maintenance of the patent in amended form, according to auxiliary request 6.

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 with the following claims and a description to be adapted thereto

   - Claims 1 to 11 filed as auxiliary request 6 with the letter dated 18 February 2020

The Registrar: The Chairman:

K. Götz-Wein A. Haderlein

Decision electronically authenticated