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Datasheet for the decision of 2 May 2022

Case Number: T 2544/16 - 3.3.01

Application Number: 10165214.7

Publication Number: 2228656

IPC: G01N33/68

Language of the proceedings: EN

Title of invention:
Quantification of allergens

Patent Proprietor:
Alk-Abelló A/S

Opponent:
Merck Patent GmbH

Headword:
Quantification of allergens/ALK-ABELLO

Relevant legal provisions:
EPC Art. 100(a), 56, 123(2)

Keyword:
Grounds for opposition - lack of patentability (yes)
Inventive step - (no)
Amendments - allowable (no)

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

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Case Number: T 2544/16 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 2 May 2022

Appellant: (Opponent)	Merck Patent GmbH Frankfurter Strasse 250 64293 Darmstadt (DE)
Respondent: (Patent Proprietor)	Alk-Abelló A/S Bøge Allé 6-8 2970 Hørsholm (DK)
Representative:	Inspicos P/S Kogle Allé 2 2970 Hørsholm (DK)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 29 September 2016 rejecting the opposition filed against European patent No. 2228656 pursuant to Article 101(2) EPC**

Composition of the Board:

Chairman	A. Lindner
Members:	T. Sommerfeld
	M. Blasi

Summary of Facts and Submissions

I. European patent 2 228 656 is based on application 10 165 214.7, which was filed as a divisional application of the earlier European patent application 06 775 965.4, itself filed as international application published as WO 2007/031080 (the "parent application"). The patent is entitled "Quantification of allergens" and was granted with 14 claims.

Claim 1 as granted reads as follows:

"1. Use of a synthetic sequence of amino acids which sequence is identical with a constant sequence to be found within a group of isoallergens of an allergen or homologous allergens to be quantified as the allergen calibration standard peptide for said group during absolute quantification of the allergen consisting of more than one isoallergen or homologous allergen by mass spectrometry, wherein said allergen calibration standard peptide is labelled with a mass-modifying functionality."

Claims 2 to 14 are dependent on claim 1.

II. Opposition was filed against the granted patent, the opponent requesting revocation of the patent in its entirety on the grounds of lack of inventive step (Article 56 EPC and Article 100(a) EPC) and of lack of sufficiency of disclosure (Article 100(b) EPC).

III. By its decision announced at oral proceedings, the opposition division rejected the opposition under Article 101(2) EPC.

IV. The opponent (appellant) lodged an appeal against that decision. With the statement of the grounds of appeal, the appellant requested that the decision of the opposition division be set aside and the patent be revoked in its entirety. It moreover requested that the patentee agree to the introduction of Article 100(c) EPC as fresh ground for opposition and submitted new documents, D37 to D39.

V. The patent proprietor (respondent) replied with letter dated 22 June 2017, requesting that opponent's appeal be dismissed and that the patent be maintained as granted (main request) or alternatively that the patent be maintained in amended form on the basis of the claims according to any of auxiliary requests 1 to 33, all filed with the letter of reply. It moreover stated that it did not consent to the introduction of Article 100(c) EPC as fresh ground for opposition and requested to hold inadmissible objections under Article 123(2) EPC insofar as these objections relate to the claims of the patent as granted or the claims of any auxiliary request where no conflicts with Article 123(2) EPC arise from the amendment(s) introduced in said claims of the auxiliary request.

VI. Summons to oral proceedings before the board were issued, as requested, followed by a communication pursuant to Article 15(1) RPBA 2020 dated 24 April 2020, providing the board's preliminary opinion on some issues. Oral proceedings were initially scheduled for 13 November 2020 but, in view of the COVID-19 pandemics, were then postponed to 9 November 2021.

VII. By letter dated 1 July 2020, the appellant informed the board that it would not attend the oral proceedings and requested a decision on the state of the file.

VIII. By letter dated 7 October 2021, the respondent announced that it would not attend the oral proceedings either.

IX. The board cancelled oral proceedings.

X. Sets of claims according to the main request (patent as granted) and according to auxiliary requests 1 to 33 are on file.

Claim 1 of auxiliary request 1 differs from claim 1 of the main request in that the alternative "homologous allergen(s)" has been deleted.

Claim 1 of auxiliary request 2 differs from claim 1 of the main request in that it specifies that the isoallergen or homologous allergen is to be quantified in an allergen sample and the allergen sample is to be selected from the group consisting of an allergen extract, an allergy vaccine, a naturally occurring and purified allergen, and a food.

Claim 1 of auxiliary request 3 differs from claim 1 of the auxiliary request 2 in that the allergen sample is to be selected from the group consisting of an allergen extract, an allergy vaccine, and a naturally occurring and purified allergen.

Claim 1 of auxiliary request 4 differs from claim 1 of the auxiliary request 2 in that the allergen sample is to be selected from the group consisting of an allergen extract and an allergy vaccine.

In claim 1 of auxiliary requests 5, 6 and 7 the amendments of auxiliary request 1 have been combined with those of auxiliary requests 2, 3 and 4, respectively.

Claim 1 of auxiliary request 8 differs from claim 1 of the main request in that it specifies that the allergen to be quantified is to be selected from the group consisting of one or more of the group of grass pollen allergens; one or more of the group of dust mite allergens; one or more of the group of weed pollen allergens; one or more of the group of birch pollen allergens; and one or more of the group of olive pollen allergens.

Claim 1 of auxiliary request 9 differs from claim 1 of the main request in that it specifies that the allergen to be quantified is selected from the group consisting of one or more of the group of grass pollen allergens; one or more of the group of dust mite allergens; and one or more of the group of birch pollen allergens.

Claim 1 of auxiliary request 10 differs from claim 1 of the main request in that it specifies that the allergen to be quantified is selected from the group consisting of Bet v 1, Aln g 1, Cor a 1, Car b 1, Que a 1, Cry j 1, Cry j 2, Cup a 1, Cup s 1, Jun a 1, Jun a 2, Jun a 3, Ole e 1, Lig v 1, Syr v 1, Pla l 1, Pla a 1, Pla a 2, Amb a 1, Amb a 2, Amb t 5, Art v 1, Art v 2, Art v 3, Par j 1, Par j 2, Par j 3, Sal k 1, Ave e 1, Cyn d 1, Cyn d 7, Dac g 1, Fes p 1, Hol l 1, Lol p 1 and 5, Pha a 1, Pas n 1, Phl p 1, Phl p 2, Phl p 3, Phl p 4, Phl p 5, Phl p 6, Poa p 1, Poa p 5, Sec c 1, Sec c 5, Sor h 1, Der f 1, Der f 2, Der f 3, Der f 7, Der p 1, Der p 2, Der p 3, Der p 7, Der m 1, Eur m 1, Eur m 2,

Gly d 1, Gly d 2, Lep d 1, Lep d 2, Blo t 1, Tyr p 2, Bla g 1, Bla g 2, Per a 1, Per a 3, Per a 7, Fel d 1, Fel d 2, Fel d 3, Fel d 4, Can f 1, Can f 2, Bos d 2, Equ c 1, Equ c 2, Equ c 3, Mus m 1, Rat n 1, Apis m 1, Api m 1, Api m 2, Ves v 1, Ves v 2, Ves v 5, Ves f 5, Ves g 5, Ves m 1, Ves m 2, Ves m 5, Ves p 5, Ves s 5, Ves v 5, Dol m 1, Dol m 2, Dol m 5, Dol a 5, Pol a 1, Pol a 2, Pol a 5, Sol i 1, Sol i 2, Sol i 3, Sol i 4, Alt a 1, Alt a 3, Alt a 4, Alt a 5, Alt a 6, Cla h 1, Cla h 2, Cla h 6, Asp f 1, Bos d 4, Mal d 1, Mal d 3, Gly m 1, Gly m 2, Gly m 3, Ara h 1, Ara h 2, Ara h 3, Ara h 4, and Ara h 5.

Claim 1 of auxiliary request 11 differs from claim 1 of the main request in that it specifies that the allergen to be quantified is selected from the group consisting of Phl p 1, Phl p 5, Phl p 6, Ole e 1, Der f 1, Der f 2, Der p 1, Der p 2, Ves v 1, Ves v 2, Ves v 5, Amb a 1, Amb a 2, Par j 1, Par o 1, Par m 1, Bet v 1, Cry j 1, and Cry j 2.

In claim 1 of auxiliary requests 12, 13, 14 and 15 the amendments of auxiliary request 1 have been combined with those of auxiliary requests 8, 9, 10 and 11, respectively.

Claim 1 of auxiliary request 16 comprises the amendments of auxiliary request 1 and further defines the synthetic sequence of amino acids as being (i) AVESYLLAHSDAYN when the allergen to be quantified is Bet v 1; ii) SAGEVEIQFR when the allergen to be quantified is Phl p 1; iii) YDAYVATLSEALR when the allergen to be quantified is Phl p 5a; iv) FDSFVASLTEALR when the allergen to be quantified is Phl p 5b; v) GKPFTLEALFDANQNTK when the allergen to be

quantified is Der f 2; and vi) GKPFQLEAVFEANQNTK when the allergen to be quantified is Der p 2.

Claim 1 of auxiliary request 17 differs from claim 1 of the main request in that it specifies that the labelling with a mass-modifying functionality uses isobaric or isomeric labelling reagents or incorporated stable isotopes.

Claim 1 of auxiliary requests 18, 19, 20 and 21 combines the amendments of auxiliary request 17 with those of auxiliary requests 1, 2, 3 and 4, respectively.

Claim 1 of auxiliary requests 22, 23 and 24 combines the amendments of auxiliary request 1 with those of auxiliary requests 19, 20 and 21, respectively.

Claim 1 of auxiliary request 25, 26, 27 and 28 combines the amendments of auxiliary request 17 with those of auxiliary requests 8, 9, 10 and 11.

Claim 1 of auxiliary requests 29, 30, 31, 32 and 33 combines the amendments of auxiliary request 17 with those of auxiliary requests 12, 13, 14, 15 and 16.

XI. The documents cited during the proceedings before the opposition division and the board include the following:

D1 Kristiansson MH et al., Rapid Commun. Mass Spectrom. 2004, 18: 1592-1598
D2 Helsper JPFG et al., J. Allergy Clin. Immunol. 2002, 110(1): 131-138
D5 US 2004/0229283
D6 US 2004/0033625

D13 van Ree R, Allergy 1997, 52: 795-805

D15 Shefcheck KJ & Musser SM, J. Agric. Food Chem. 2004, 52: 2785-2790

D19 Hakkaart GAJ et al., Clinical and Experimental Allergy 1998, 28: 169-174

D30 "Allergen Nomenclature" WHO/IUIS Allergen Nomenclature Subcommittee; J Allergy Clin. Immunol. 1995, 96(1): 5-14

D31 Heck AJR & Krijgsveld J, Expert Rev. Proteomics 2004, 1(3): 317-326

D33 Guerrera IC & Kleiner O, Bioscience Reports 2005, 25 (1/2): 71-93

XII. The appellant's submissions, in so far as they are relevant to the present decision, may be summarised as follows:

Document D13 could be considered the closest prior art. It disclosed the use of antibody-based analytical methods for the quantification of allergens in a sample. It moreover addressed the issue of different isoforms or homologues of an allergen (section bridging pages 798 and 799), and concluded that one should select antibodies that recognised the whole spectrum of isoforms (page 799, left column, third paragraph). The difference between the subject-matter claimed in the patent as granted and D13 was the use of mass spectrometry. Since there was no indication of a level of detection in the examples of the patent, the objective technical problem had to be formulated as the provision of an alternative analytical method that overcame the disadvantages inherent to the use of antibodies. Consideration of mass spectrometry as a solution to the problem was obvious. Document D31, representative of the common general knowledge at the time, explained that the need for alternative methods

for accurate measurement of protein quantification was due, *inter alia*, to the shortcomings of antibody-based technologies and that the introduction of stable isotope-labeling approaches had dramatically changed this (D31, page 323, first paragraph). Likewise, also D33 reviewed the application of mass spectrometry in proteomics (D33, title on page 71, page 77 section "Quantitative Mass spectrometry" onwards). Hence, the skilled person would have been motivated to replace antibody-based assays by mass spectrometry, which implied the use of calibration standard peptides. As to the detection of allergen isoforms, documents D5 and D6 (paragraphs [0021], [0071] and [0079], Example IV: paragraphs [0108] and [0109], claim 14) specifically taught that the methods could be used to detect and quantify splicing and other isoforms. Moreover, D6 disclosed that one of the advantages of the method was that it obviated the need for antibodies or other reagents that were specific for a particular protein (paragraph [0082]). The fact that mass spectrometric methods were predominantly developed for proteomics would not have deterred the skilled person from using them for quantification of allergens, which were also "ordinary" proteins. The same arguments applied to the dependent claims, which merely set out certain allergens which were known to comprise isoforms, as was evident from D30. Document D19 specifically related to the quantification of the major dust mite antigen Der p 2 and its isoforms and, like D13, also taught to use non-discriminating monoclonal antibodies (page 173, last paragraph of the section "Discussion").

XIII. The respondent's arguments, in so far as they are relevant to the present decision, may be summarised as follows:

Document D13 could be considered the closest prior art. The distinguishing feature of the subject-matter claimed in the patent was the use of quantitative mass spectrometry (qMS) using a common peptide instead of a monoclonal antibody-based ELISA. The objective technical problem to be solved was to provide an improved quantitative determination of a group of immunologically related species of the same generic peptide. The feature of using a "common peptide" was absent from the prior art, including both D5 and D6. Hence, even if it was accepted that qMS could be considered an obvious alternative to the existing immune assays, it would still not have been possible to arrive at the claimed invention without further modifying the combined teachings of D13, D5 and D6. As for D6, paragraph [0071] suggested to quantify splice isoforms of proteins, but did not provide any direct and unambiguous disclosure of a peptide which was found in all splice isoforms (single "common peptide"). Additionally, splice isoforms, which consisted of different expression products from the same gene, typically exhibiting size variations, were not equivalent to isoallergens, which were expression products from related genes in different individual organisms. So D6 did not provide the suggestion to quantitatively determine amounts of proteins that were related in the same way as isoallergens were. None of the further references cited by the appellant provided for the missing feature of using a peptide common for a group of isoallergens.

The sets of claims of auxiliary requests 10, 11, 14 to 16, 27, 28 and 31 to 33 provided increasingly specific definitions of allergens to be determined and therefore were further distinct over a number of references cited by the appellant. In particular D1 did not relate to

any of the allergens recited in the claims of any of these requests.

The sets of claims of auxiliary requests 2 to 9 and 19 to 24 provided narrow definitions of the allergen sample to be determined in contrast to e.g. D5 and D6 which merely related to "some source". Therefore these auxiliary claim requests clearly distinguished the technical field of the invention (quantification of allergens in potentially allergenic commercial products) from the technical field of D6 (proteomics).

The sets of claims of auxiliary requests 17 to 33, which related to qMS using specifically defined mass modifying labels, recited subject-matter which was not to be found in e.g. D2. This meant that any combination with D5 and D6 would not have led to the claimed subject matter.

Reasons for the Decision

1. The appeal is admissible.

Main request (patent as granted)

2. Inventive step

2.1 The present patent discloses a method for absolute quantification of allergens consisting of more than one isoallergen or homologous allergen by mass spectrometry (MS) making use of a synthetic sequence of amino acids which is identical to a constant sequence to be found

within the group of isoallergens or homologous allergens to be quantified (paragraph [0020]). According to paragraph [0005] of the patent, "[k]nowledge of the composition of the extracts and the content of essential allergens is a prerequisite for reproducibility, safety and efficacy of the final product [the commercial allergen vaccines]", but "[a] major challenge in the manufacture of allergen vaccines is standardisation, i.e. securing a constant potency from batch to batch". Moreover, "[a]lso in the food industry routine high-through-put techniques for reliable detection and quantification of food allergens is necessary" (paragraph [0008]). "The method according to the invention is useful e.g. in a release assay in order to ensure a safe and accurate amount of allergen during production of a vaccine" (paragraph [0019]).

2.2 Document D13, which is a review article on analytic aspects of the standardisation of allergenic extracts (see Title), can be taken as the closest prior art. It discloses the use of allergen-specific monoclonal antibodies (mAbs) for quantifying antigens using ELISA and furthermore teaches that "For standardization, one should select mAbs that recognize the whole spectrum of isoforms. Alternatively, a mixture of two or more different mAbs could be used to ensure complete coverage of isoforms" (page 799, left column, third paragraph). The claimed method differs from the method disclosed in D13 in that mass spectrometry is used instead of ELISA. Linked to the different assay used, the claimed method uses an allergen calibration standard peptide that is found in a group of isoallergens or homologous allergens.

2.3 There is no data in the patent or elsewhere on file comparing the performance of the method of the prior

art (ELISA) with that of the claimed method using quantitative mass spectrometry (qMS). However, the patent refers in paragraph [0006], last sentence, to the disadvantages of using techniques that are dependent on antibodies as reagents, since they are "vulnerable to change over time". Other disadvantages related to the use of antibodies in the detection of food allergens had also already been acknowledged in the prior art (e.g. D15, page 2785, right column, first paragraph). Hence the board considers that the objective technical problem has to be formulated as the provision of a further allergen analytical method that overcomes the disadvantages inherent to the use of antibodies. The solution is the method as claimed, and the board considers that it credibly solves the problem set out above.

2.4 The patent itself acknowledges that mass spectrometry methods were well known for use "for quantification of a variety of biomolecules from complex mixtures such as plasma, cell and tissue samples" (paragraph [0009]) and refers to a number of prior art documents in the subsequent paragraphs. The use of mass spectrometry for quantification of proteins is reviewed in D31 and D33, e.g., and D31 also explains in its introductory section that the need for alternative methods for accurate measurement of protein quantification was due, *inter alia*, to the shortcomings of antibody-based technologies, which protein expression quantification had traditionally relied upon (D31, page 317, right column, second paragraph). Hence, the board considers that the skilled person, motivated to provide methods for allergen quantification without the problems of antibody-based methods, would have followed the prevalent teaching of the prior art, represented e.g. by D31, and would have used mass spectrometry methods

instead. The specific use of an allergen calibration standard peptide that is found in a group of isoallergens or homologous allergens would have been the obvious consequence of replacing ELISA in D13 by mass spectrometry, since it is the equivalent of using "mAbs that recognize the whole spectrum of isoforms" (D13, supra) in the context of mass spectrometry. The board thus considers that the claimed solution is obvious from the disclosure of D13 combined with common general knowledge as represented by e.g. D31.

2.5 The respondent defined the objective technical problem as being the provision of an improved quantitative determination of a group of immunologically related species of the same generic peptide. As explained above, however, the board fails to see any evidence of any improvement in terms of quantitative determination; in this context and for the same reasons, the board also disagrees that the objective technical problem is the provision of a more sensitive quantitative determination of the allergens measured, as was formulated by the opposition division.

2.6 The respondent also argued that the feature of a "common peptide" as the calibration peptide in a qMS is not disclosed in the prior art, also not in D5 or D6. The board again disagrees. As explained above, the use of a "common peptide" in qMS would be the equivalent to using "mAbs that recognize the whole spectrum of isoforms" in antibody-based methods. Moreover, document D6, which discloses the use of mass spectrometry for protein quantification and also discusses the advantages of using mass spectrometry methods over antibody-based assays for protein quantification (paragraph [0082]), teaches how to use the method for

quantification of protein splice variants by choosing a peptide which is common to all splice variants (Example IV, paragraph [0109]). This is further elaborated in paragraph [0071] which reads: "In the case of splice variants, peptide standards can be selected to assess a common portion as well as a portion of the sequence in which the splice isoforms differs, if desired. Thus, the invention provides a method for the quantitative profiling of splice and other protein isoforms. The invention also provides a method for the determination of the absolute quantities of splice and other protein isoforms", emphasis added by the board. The peptide standard which is selected to assess a common portion of the splice isoforms corresponds to the allergen calibration standard peptide that is "found in a group of isoallergens or homologous allergens" of the claimed subject-matter. Albeit the sentence at paragraph [0071] of D6 may not provide, as argued by the respondent, a disclosure of a peptide that is found in all splice isoforms, it would be obvious for the skilled person that when aiming at determining all splice isoforms such a peptide would have to be used. The board notes that the claim itself refers to a "group of homologous allergens or isoallergens", so not necessarily all homologous allergens or isoallergens. Also the fact that splice isoforms are different to isoallergens and may have different sizes does not have an impact on the applicability of the method disclosed in D6 to the latter ones: all that is required is that there is a common sequence, which is the case both for splice isoforms and for isoallergens.

2.7 The main request is thus not allowable for lack of inventive step. Accordingly, the ground of opposition under Article 100(a) EPC, in combination with

Article 56 EPC, prejudices the maintenance of the patent as granted.

3. Auxiliary request 1 - inventive step

3.1 Claim 1 of this request differs from claim 1 of the main request merely in that the alternative "homologous allergen(s)" was deleted.

3.2 According to the respondent, this amendment was made in reaction to objections of insufficiency of disclosure for embodiments relating to homologous allergens; no arguments were provided concerning inventive step.

3.3 Hence, this amendment per se does not contribute for inventive step. Auxiliary request 1 is not allowable for lack of compliance with Article 56 EPC.

4. Auxiliary requests 2 to 7 - inventive step

4.1 Claim 1 of these requests specifies the allergen samples that are to be used.

4.2 The respondent argued that the claims of these auxiliary requests provide increasingly specific definitions of allergen samples to be determined, thus further distinguishing from the prior art, thereby clearly delimiting the technical field of the claimed invention (quantification of allergens in potentially allergenic commercial products) from the technical field of D6 (proteomics).

4.3 The board again notes that, while indeed D6 is not specifically related to quantification of allergens, still it is directed to the broader field of protein quantification. As explained above, the skilled person

would have had no reasons to doubt that the teachings of D6 (and D31) could also be applied to quantification of any kind of proteins, including allergens, i.e. proteins with allergenic potential, and would therefore have used this method for quantification of allergens in allergen samples.

4.4 Auxiliary requests 2 to 7 are thus also considered to contravene Article 56 EPC.

5. Auxiliary requests 8 and 9 - inventive step

5.1 Claim 1 of these requests specifies the groups of allergens to be quantified.

5.2 The board fails to see how these amendments, which just define the allergens to be quantified as belonging to well-known allergen groups, can contribute for inventive step.

5.3 Accordingly, auxiliary requests 8 and 9 are also considered to contravene Article 56 EPC.

6. Auxiliary requests 10 and 11 - inventive step

6.1 Claim 1 of these requests identifies the specific allergens to be quantified.

6.2 According to the respondent, these amendments were made "in the event the Board should concur with the Opponent on the relevance of reference D1 in the inventive step considerations" (reply to the statement of grounds of appeal, page 4, fourth paragraph).

6.3 The board does not rely on document D1 for the conclusions on inventive step. Rather the board still

considers document D13 to be the closest prior art and notes that at least some of the allergens listed in the claims of auxiliary requests 10 and 11 were known to belong to allergen groups that comprise isoallergens, as described in D30. As argued by the appellant (statement of grounds of appeal, page 32, second paragraph), given that all these allergens are simply proteins and only have this inherent property as a common denominator, applying the obvious teaching to these particular embodiments does not involve an inventive step either. Document D19, which deals with isoforms of the major house dust mite allergen Der p 2, and also teaches that it is preferable to use non-discriminating mAbs over isoform specific mAbs (D19, page 173, last paragraph of the section "Discussion") is moreover detrimental for inventive step of subject-matter explicitly directed to this allergen (or to house dust mite allergens in general).

6.4 Hence auxiliary requests 10 and 11 are also considered to contravene Article 56 EPC.

7. Auxiliary requests 12 to 15 - inventive step

7.1 Claim 1 of these requests combines the amendments of auxiliary request 1 with those of auxiliary requests 8 to 11, respectively.

7.2 Accordingly, for the same reasons as set out above in relation to auxiliary requests 1 and 8 to 11, these requests are also considered not to involve an inventive step and are therefore not allowable for lack of compliance with Article 56 EPC.

8. Auxiliary request 16 - added subject-matter and inventive step

8.1 As indicated by the respondent (letter of reply, dated 22 June 2017, page 3), the claims of auxiliary request 16 have been amended by limiting claim 1 to the subject matter of the Examples and Figure 2, i.e. by restricting the claims to use of specific peptides to quantify specific allergens. Hence the amendments introduced to claim 1 of auxiliary request 16 are not based on the claims as granted.

8.2 The board notes that the Examples either disclose the production of the synthetic calibration peptides but not their use for allergen quantification (Examples 1 to 5) or their use for absolute quantification of isoallergens employing the AQUA strategy (Example 7). Since claim 1 of auxiliary request 16 is not limited to quantification using the AQUA strategy, the board considers that the claimed subject-matter is an unallowable intermediate generalisation and therefore the amendments add subject-matter.

8.3 Accordingly, the board comes to the conclusion that auxiliary request 16 is not allowable for lack of compliance with Article 123(2) EPC.

8.4 Additionally, the board fails to see how the amendments contribute for inventive step. The respondent merely stated (reply to grounds of appeal, page 13, paragraph 6) that "Auxiliary requests 10, 11, 14-16, 27, 28, and 31-33, provide increasingly specific definitions of allergens to be determined. As such the claims provide distinction over a number of references cited by the Appellant, in particular those cited on page 31 in the grounds for opposition". Even if the allergens to be determined may be a further distinction to the documents of the prior art, this is not necessarily

sufficient to acknowledge inventive step, as was concluded above in relation to auxiliary requests 10 and 11 (section 6.).

8.5 Hence, auxiliary request 16 is considered not allowable also for lack of compliance with Article 56 EPC.

9. Auxiliary requests 17 to 33 - added subject-matter and inventive step

9.1 In all these requests claim 1 has been amended to specify that the labelling with a mass-modifying functionality uses isobaric or isomeric labelling reagents or incorporated stable isotopes. As basis for this amendment, the respondent has indicated page 18, lines 19 to 21, and page 19, lines 7 to 11, of the application as filed. According to the respondent, this feature is not to be found e.g. in D2, meaning that any combination with D13, D5 and D6 would not lead to the claimed subject-matter.

9.2 The indicated passages of the application as filed read respectively: "According to this embodiment of the invention, the labelling of the degraded allergen sample and/or the calibration standard peptides is performed by set of isomeric or isobaric labelling reagents such as iTRAQ^{TM} Reagents (Applied Biosystems, Foster City, CA, USA)" and "Another method for labelling in connection with quantification of proteins using MS techniques are e.g. the AQUA technique using internal calibration peptides synthesized with incorporated stable isotopes (^{13}C, ^{15}N) to mimic native peptides formed by enzymatic digestion using e.g., trypsin (...)". The board fails to see how these very specific disclosures of the application as filed can provide basis for the amendments introduced into claim

1 of auxiliary requests 17 to 33, let alone in combination with the other features of the claim. The claimed subject-matter is thus considered to constitute an unallowable intermediate generalisation.

9.3 Moreover, the board notes that document D2 was mentioned by the appellant on page 31, second paragraph, of the grounds of appeal, as one among a list of prior art documents cited to show that "scientists working in the field of allergy and immunotherapy had already turned to mass spectrometry for both qualitative and quantitative analyses". Apart from the statement that this feature is not present in D2, the respondent failed to indicate how this amendment is to contribute for inventive step. The board notes that the patent discloses the use of isobaric labeling reagents or isotopic labeling with incorporated stable isotopes as mere alternatives, known from the prior art, of mass modifying labels to be used in quantitative mass spectrometry (e.g. paragraphs [0010], [0012], [0013], [0089] of the patent), and, according to the appellant (statement of grounds of appeal, page 25, second paragraph), several of these labeled synthetic peptides were commercially available at the time.

9.4 The board thus considers that the claims of auxiliary requests 17 to 33 do not comply with Article 123(2) EPC and do not appear to overcome the objections for lack of inventive step. Hence, auxiliary requests 17 to 33 are not allowable for lack of compliance with Articles 123(2) and 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated