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Datasheet for the decision of 17 October 2024

Case Number: T 1593/22 - 3.3.05

Application Number: 14713926.5

Publication Number: 2969098

IPC: B01D15/20, B01D15/38, C07K16/00, C07K1/22

Language of the proceedings: EN

Title of invention:
METHODS FOR PURIFYING ANTIBODIES

Patent Proprietor:
GlaxoSmithKline Intellectual Property Development Limited

Opponent:
WALLINGER RICKER SCHLOTTER TOSTMANN

Headword:
Purifying antibodies/GSK

Relevant legal provisions:
EPC Art. 123(2)
RPBA 2020 Art. 11

Keyword:
Amendments - allowable (yes)
Remittal - special reasons for remittal (yes)

Decisions cited:
T 0201/83, T 0962/98, T 1238/08, T 1556/16

Catchword:

Europäisches Patentamt
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Office européen des brevets

Beschwerdekammern

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Case Number: T 1593/22 - 3.3.05

D E C I S I O N
of Technical Board of Appeal 3.3.05
of 17 October 2024

Appellant: (Patent Proprietor)	GlaxoSmithKline Intellectual Property Development Limited 980 Great West Road Brentford Middlesex TW8 9GS (GB)
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Representative:	Oetke, Cornelia Wallinger Ricker Schlotter Tostmann Patent- und Rechtsanwälte Partnerschaft mbB Zweibrückenstraße 5-7 80331 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 7 April 2022 revoking European patent No. 2969098 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chair	E. Bendl
Members:	G. Glod
	O. Loizou

Summary of Facts and Submissions

I. The appeal is by the patent proprietor (appellant) and concerns the opposition division's decision revoking European patent No. 2969098.

II. The opposition division decided that none of the requests, that is to say the main request (patent as granted) and auxiliary requests 1 to 31, were allowable, in some cases under Article 123(2) EPC and in the others under Article 123(3) EPC.

III. During oral proceedings before the board on 17 October 2024, the appellant only maintained auxiliary requests 6, 7, 16, 17, 23, 24, 30 and 31, and withdrew all the other requests.

IV. Claim 1 of what is now the main request (filed as auxiliary request 6) reads as follows.

"*1. A method for purifying a protein, from a solution containing at least one host cell contaminant comprising: a) adsorbing the protein to Protein A, Protein G, or Protein L immobilized on a solid support; b) removing the at least one host cell contaminant by contacting the solid support containing the adsorbed protein with a first wash buffer comprising an aliphatic carboxylate, wherein said aliphatic carboxylate comprises a 6-12 carbon backbone; and c) eluting the protein from the solid support, wherein the solution is a cell culture feedstream, wherein the at least one host cell contaminant is a host cell protein or host cell DNA, wherein the protein is selected from one of: antibody, antibody fragment, immunoglobulin single variable domain, Fab, F(ab')2, Fv, disulphide*

linked Fv, scFv, disulphide-linked scFv, or diabody, wherein the aliphatic carboxylate is selected from one of: caproate, heptanoate, caprylate and decanoate, wherein the source of the aliphatic carboxylate is selected from an aliphatic carboxylic acid, a sodium salt of an aliphatic carboxylic acid, or a potassium salt of an aliphatic carboxylic acid, and wherein when the aliphatic carboxylate is sodium caprylate, the concentration of sodium caprylate is between 50 to 125 mM."

Claims 2 to 13 directly or indirectly refer to claim 1.

V. The respondent's (opponent's) arguments, where relevant to the decision, can be summarised as follows.

The requirements of Article 123(2) EPC were not fulfilled.

In particular, steps b) and c) of claim 1 now related to the solid support. Claim 1 explicitly required elution from the solid support, which made technical sense. Claim 1 did not require elution from Protein A, G or L. This was different from the original disclosure, which referred to the superantigen. Claim 1 did not exclude the presence of a further elution step. Furthermore, the solid support and Protein A, Protein G, or Protein L were different entities.

If the board did not agree with the opposition division's conclusion, the case should be remitted to the opposition division so that it could deal with all the issues it had not yet decided upon, including outstanding objections under Article 123(2) EPC.

The value of 50 mM could not be derived from example 3, and multiple selections from multiple lists had to be made in order to arrive at the feature "when the aliphatic carboxylate is sodium caprylate, the concentration of sodium caprylate is between 50 to 125 mM." The experimental set-up of example 3 was very specific, so it was not possible to isolate only 50 mM sodium caprylate from it. Example 3 lacked a control, so it was not possible to conclude that 50 mM sodium caprylate was an effective concentration. It appeared that the example with 50 mM sodium caprylate was a non-working embodiment. In addition, 50 mM was a selection from four concentrations. Limiting the sodium caprylate concentration without limiting the sodium decanoate and sodium dodecanoate concentration, while simultaneously limiting the claims to these sources of aliphatic carboxylates, was also a selection.

The conditions set out in T 201/83 for limiting a concentration range were not fulfilled.

VI. The appellant agreed with the respondent's position on remittal. The appellant's further arguments are reflected in the reasoning below.

VII. The appellant (patent proprietor) requested that the decision under appeal be set aside and that the patent be maintained in amended form on the basis of the main request (previously filed as auxiliary request 6) or on the basis of one of auxiliary requests 7, 16, 17, 23, 24, 30 or 31, which together formed the basis of the decision under appeal.

The respondent (opponent) requested that the appeal be dismissed.

Reasons for the Decision

Main request

1. Claim interpretation

1.1 Claim 1 relates to a purification method for a protein. In step a) the protein is adsorbed to a specified Protein A, G or L, which is immobilised on a solid support. It is evident to the skilled person that the objective of this step is to ensure that the protein to be purified interacts with the specified Protein A, G or L so that it is not washed out. The skilled person also knows that non-specific binding to the solid support may occur to some degree, but it is certainly not the objective of step a).

1.2 In step b) the solid support containing the adsorbed proteins is contacted with a wash buffer to remove the contaminant(s). Since step a) mentions adsorption to the specified Protein A, G or L, it is evident that the adsorbed proteins referred to in step b) are those proteins (to be purified) that are adsorbed to Protein A, G or L, which is itself on the solid support. The other components, which are not to be purified, are to be removed in this washing step b). The skilled person will undoubtedly understand that the goal of this washing step is to remove the contaminants from the solid support, which includes Protein A, G, or L immobilised thereon. The first wash buffer has to be chosen accordingly. Any protein to be purified which is only adsorbed to the solid support by non-specific bonding is expected to be washed out in this step as well.

1.3 In step c) the protein is eluted from the solid support. The skilled person reading the claim in context will understand that the protein is eluted from Protein A, G or L, which is immobilised on the solid support. The goal of the method claimed is to purify a protein. Since the protein is adsorbed in step a) as a result of specific binding, the elution step has to aim to recover the protein by removing it from Protein A, G or L, which is part of the solid support. Therefore step c) in fact relates to elution of the protein (to be purified) from Protein A, G or L. Some protein to be purified that is still adsorbed to the solid support by non-specific bonding may also be eluted in step c).

1.4 This interpretation is more or less in line with the opposition division's interpretation 2 (point 11.5 of the decision). Interpretation 1 is certainly literally possible, but is not considered to be technically relevant. It is evident from step a) that Protein A, G or L is on the solid support and specifically binds the protein to be purified. Where there is a mention of protein to be purified on the solid support, the skilled person will immediately understand that the protein to be purified is on Protein A, G or L, which is itself on the solid support. A distinction would not be made in that context. It is true that other steps may be present in the claimed method. However, an interpretation which supports the idea that the elution step would only remove the protein to be purified from the solid support and not from Protein A, G or L would mean that no protein was purified. This would be contrary to the aim of the method, and would imply that an essential step was missing from claim 1. Such an understanding is rather theoretical and formalistic, and is not in line with a skilled person's reading.

2. Article 123(2) EPC

The requirements of Article 123(2) EPC are met, for the following reasons.

2.1 The feature under debate, which led to the opposition division's decision, is "eluting the protein from the solid support".

Claim 1 as originally filed explicitly discloses "eluting the protein from the superantigen immobilized on the solid support". Claim 1 of the present request now specifies the superantigen as Protein A, G, or L. In view of the interpretation given above (point 1.3), step c) of this request has the same meaning as step c) of the application as filed. Nor does claim 1 as originally filed exclude the possibility that, during the elution step c), protein to be purified which is still adsorbed to the solid support by non-specific bonding is also eluted. "[A]ny other suitable material" (page 10, line 23 of the application as originally filed) is understood as any material that is suitable for Protein A to adhere to (see page 10, line 20). It is not understood as a material which specifically interacts with the protein to be purified. Therefore, the omission of the expression "Protein A, Protein G, or Protein L immobilised on" from step c) of claim 1 does not lead to a deficiency under Article 123(2) EPC.

The respondent also objected to step b) because it was different from step b) as originally filed ("*contacting the immobilized superantigen*"), and thus implied a different wash buffer. In view of the interpretation given above (point 1.2), no difference between step b)

of this request and step b) of claim 1 as originally filed can be identified.

2.2 The feature "*when the aliphatic carboxylate is sodium caprylate, the concentration of sodium caprylate is between 50 to 125 mM*" is also directly and unambiguously derivable from the application as originally filed, for the following reasons.

Specifying the aliphatic carboxylate as sodium caprylate with a specific concentration range is based on page 11, lines 13 to 19 of the application as originally filed. A specific selection cannot be identified. The aliphatic carboxylate of claim 1 is not limited to sodium caprylate: claim 1 only contains a specification for the particular case when the aliphatic carboxylate is sodium caprylate. There is no disclosure implying that in such a case the other carboxylates would have to be sodium decanoate or sodium dodecanoate. Different options are given on page 11, of which one has now been further defined.

Claim 1 now contains 50 mM as the lower limit for the concentration of sodium caprylate. It is undisputed that this value is only disclosed in Table 5 in the context of a specific example. It is necessary to assess whether the value can be extracted from the example and used for delimiting the already existing range without violating Article 123(2) EPC.

According to established case law (Case Law of the Boards of Appeal of the EPO, 10th edition, 2022, II.E. 1.5.2 and in particular T 201/83) an amendment of a concentration range in a claim for a mixture is allowable on the basis of a particular value described in a specific example, provided the skilled person

could have readily recognised this value as not so closely associated with the other features of the example as to determine the effect of that embodiment of the invention as a whole in a unique manner and to a significant degree. In the case at hand, example 3 relates to the effect of caprylate concentration on impurity clearance. It is accepted that the results shown in figures 1 and 2 are specific to the defined washing composition used (i.e. buffer, pH). However, the skilled person would also have recognised from example 3 that the caprylate concentration is crucial for impurity clearance (see title of example 3 and page 19, lines 10 to 12 of the application as originally filed). Although this effect was shown in a very specific example (specific buffers, pH), the general teaching of the example is that the concentration of sodium caprylate is highly important. It is recognised that the effect of caprylate concentration would also be present with different wash buffers, but possibly to a different degree. Therefore the skilled person would infer that the value of 50 mM sodium caprylate is not so closely associated with the other features of the example as to determine the effect in a unique manner and to a significant degree. Consequently, in the case at hand, the value of 50 mM sodium caprylate can be isolated from the example and combined with the more general range of 10 mM to 125 mM disclosed in the description. In view of the results of example 3, the skilled person would also have recognised that 50 mM to 125 mM is preferred over 10 mM to 125 mM. All the concentrations used in example 3 (25 mM, 50 mM, 75 mM, 100 mM) are considered preferable to the lower limit (10 mM) of the generally disclosed range. Restricting the range does not lead to the singling out of a specific value. A specific selection cannot be identified.

In the case at hand, the fact that the wash buffer comprising 50 mM sodium caprylate is not the best-performing buffer is irrelevant to the question of Article 123(2) EPC, but may be relevant to the question of inventive step. What matters is whether the skilled person would have inferred that the concentration of sodium caprylate is generally important for the performance of the wash buffer. This is indeed the case, for the reasons set out above.

T 962/98 and T 1238/08, which were relied on by the respondent, are not relevant to the case at hand, since they do not relate to the amendment of an explicitly disclosed range (in this case 10 mM to 125 mM) by a value disclosed in an example (in this case 50 mM).

The situation here is similar to the one described in T 1556/16 (Reasons 21). As set out above, the skilled person will understand that the range 50 mM to 125 mM sodium caprylate is certainly preferred to the originally disclosed range of 10 mM to 125 mM.

2.3 The subject-matter of claim 8, which refers to claim 7, is directly and unambiguously derivable from the application as filed (page 12, lines 8 to 10 and 21 to 22, and claims 22 and 25). The general disclosure in lines 8 to 10 is further specified in lines 21 and 22 without leading to the singling out of a specific combination. Therefore no new subject-matter is created.

3. Article 111(1) EPC and Article 11 RPBA

The EPC does not guarantee parties an absolute right to have every aspect of fact or of law on which a board of

appeal bases its decision examined at two instances (Case Law of the Boards of Appeal of the EPO, 10th edition, 2022, V.A.9.2.1).

In the case at hand, Article 123(2) EPC was part of the impugned decision, and all the aspects relating to Article 123(2) EPC were discussed in the reply to the appeal. The board also dealt with all these issues in the communication under Article 15(1) RPBA. The board held that it could decide on all the issues under Article 123(2) EPC without undue burden (see point 2 above). The board therefore decided not to remit the case so that the opposition division could deal with issues under Article 123(2) EPC not yet decided upon at opposition, as initially requested by both parties.

The situation is different for the requirements under Articles 54, 56 and 83 EPC. These articles were not part of the impugned decision. Consequently, the board would have to conduct a complete analysis in respect of these, which would be contrary to the main purpose of the appeal proceedings, i.e. a review of the decision under appeal. In line with established case law (Case Law of the Boards of Appeal of the EPO, 10th edition, 2022, V.A.9.3), this qualifies as special reasons justifying a remittal to the opposition division. Therefore, and in agreement with the parties' requests, the case is remitted to the opposition division so that these outstanding issues can be dealt with.

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 for further prosecution.

The Registrar: The Chairman:

C. Vodz E. Bendl

Decision electronically authenticated