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Datasheet for the decision of 28 November 2024

Case Number: T 2192/22 - 3.3.04

Application Number: 10798291.0

Publication Number: 2513135

IPC: C07K1/22, C12N9/64

Language of the proceedings: EN

Title of invention:
Method Of Purifying Polypeptides

Patent Proprietor:
CSL Limited

Opponent:
Maiwald GmbH

Headword:
Purifiying polypeptides/CSL

Relevant legal provisions:
EPC Art. 54
EPC R. 139

Keyword:
Novelty - main request (no) - auxiliary request (yes)
Category of granted claims
Second non-medical use (no)
Correction of error in document(s) - (no)

Decisions cited:
G 0002/88, G 0006/88, T 0140/94, T 0332/94, T 0892/94, T 0319/98, T 0966/00, T 0681/01, T 0593/06, T 1179/07, T 0022/09, T 1626/16, T 1913/21, T 0149/22

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Case Number: T 2192/22 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 28 November 2024

Appellant: (Patent Proprietor)	CSL Limited 655 Elizabeth Street Melbourne VIC 3000 (AU)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Appellant: (Opponent)	Maiwald GmbH Elisenhof Elisenstr. 3 80335 München (DE)
Representative:	Maiwald GmbH Elisenhof Elisenstraße 3 80335 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 13 July 2022 concerning maintenance of the European Patent No. 2513135 in amended form.**

Composition of the Board:

Chairwoman	M. Pregetter
Members:	A. Chakravarty
	A. Bacchin

Summary of Facts and Submissions

I. In an interlocutory decision, the opposition division decided that European patent EP 2 513 135, entitled "Method Of Purifying Polypeptides", amended according to auxiliary request 4 and the invention to which it related met the requirements of the EPC.

II. Both the patent proprietor and the opponent (appellants I and II, respectively) filed appeals against the opposition division's decision.

III. In the decision under appeal, the opposition division held that claim 1 of the patent as granted (main request) lacked novelty in view of the disclosure in documents D2 to D6 and D10 (see point XI. below for document numbering). Claim 1 of auxiliary requests 1 and 2 also lacked novelty for the same reasons as the main request. Claim 1 of auxiliary request 3 was held to lack novelty in view of the disclosure in documents D3 to D5.

IV. In relation to auxiliary request 4, the opposition division dismissed objections under Article 123(3) EPC, Article 83 EPC, Article 84 EPC, Article 54 EPC and Article 56 EPC.

V. Both appellants submitted statements of grounds of appeal and replies thereto.

VI. In its statement of grounds of appeal, the patent proprietor *inter alia* requested that the decision under appeal be set aside and that the patent be maintained as granted (main request). Alternatively, that the patent be maintained on the basis of the set of claims

of one of auxiliary requests 1 to 3, as filed with the letter dated 18 June 2021. Further alternatively, that the patent be maintained on the basis of the set of claims of auxiliary request 4, as filed with the letter dated 18 June 2021 (meaning a dismissal of the opponent's appeal), or on the basis of one of the sets of claims of auxiliary requests 5 to 41, as filed with the letter dated 18 June 2021 or auxiliary requests 42 to 67, as filed with the letter dated 14 April 2022.

VII. The board issued a communication under Article 15(1) RPBA setting out its preliminary opinion on the appeals. In this communication it informed the parties that, in claim 1 of auxiliary request 4, the claimed "use" was to be understood as the "use" in a process of purification of a polypeptide of interest by cation-exchange chromatography and that, as such, the claim related to the whole process for producing the purified polypeptide. Said process was characterised by the process/method steps defined in the claim and "reduction of host cell proteins" was a functional feature of the claimed process. It further noted that the question of whether or not the claimed subject-matter related to a process for production or to the use of a substance for achieving an effect may play a role in its considerations on novelty.

VIII. Appellant I submitted two further letters in reply to the board's communication, one dated 11 November 2024 and one dated 26 November 2024. With this second letter, it withdrew the former main request and auxiliary requests 1 to 3, 12, 21, 42, 48, and 54. Accordingly, previous auxiliary request 4 became the main request and the remaining claim requests were renumbered as auxiliary requests 1 to 58 (auxiliary requests 1 to 7, corresponding to previous auxiliary

requests 4 to 11; auxiliary requests 8 to 15, corresponding to previous auxiliary requests 13 to 20; auxiliary requests 16 to 35 corresponding to previous auxiliary requests 22 to 41; auxiliary requests 36 to 58 corresponding to previous auxiliary requests 43 to 47, 49 to 53 and 55 to 67).

IX. Oral proceedings were held as requested by the parties. During the oral proceedings, appellant I requested that auxiliary request 24 (which had been filed as auxiliary request 30) be renumbered as auxiliary request 1, with consequent renumbering of the remaining auxiliary requests on file.

X. At the end of the oral proceedings, the chair announced the board's decision.

XI. The following documents are referred to in this decision.

D1: WO 2011/073235 (application as filed),

D2: Arakawa *et al.* (2007) The effects of arginine on protein binding and elution in hydrophobic interaction and ion-exchange chromatography. Protein Expression and Purification, 54, 110-116,

D3: WO 99/31120, A1

D4: WO 03/042344, A2

D5: WO 2006/127284, A2

D6: US 4,828,990

D7: WO 2009/149067, A1

D8: WO 01/72844, A2

D9: WO 98/21234, A2

D10: WO 2009/099829, A1

XII. Claim 1 of the main request request reads:

"1. Use of a chemical compound for the reduction of host cell proteins in the purification of a polypeptide of interest by cation-exchange chromatography wherein the chemical compound is added in a concentration of at least 7 mM

a) to an equilibration fluid of the cation-exchange matrix wherein the equilibration fluid is adjusted such that at least part of the chemical compound in the equilibration fluid binds to the cation-exchange matrix due to a charge that is opposite to the charge of the cation-exchange matrix

and/or

b) to a loading fluid which is applied to the cation-exchange matrix and which comprises the polypeptide of interest wherein the loading fluid is adjusted such that at least part of the chemical compound and at least part of the polypeptide of interest in the loading fluid bind to the cation-exchange matrix due to a charge that is opposite to the charge of the cation-exchange matrix

and/or

c) to a washing fluid which is used to wash the cation-exchange matrix once the polypeptide of interest has bound to the cation-exchange matrix due to a charge that is opposite to the charge of the cation-exchange matrix wherein the washing fluid is adjusted such that at least part of the chemical compound in the washing fluid binds to the cation-exchange matrix due to a charge that is opposite to the charge of the cation-exchange matrix and that at least part of the polypeptide of interest and at least part of the already bound chemical compound if added at step a) or b) continue to bind to the cation-exchange matrix due to a charge that is opposite to the charge of the cation-exchange matrix

thereby increasing the amount of the polypeptide of interest bound to the cation-exchange matrix relative to the amount of host cell proteins bound to the cation-exchange matrix before the cation-exchange matrix is eluted and thereby leading to an increased ratio of the polypeptide of interest to host cell proteins in the eluate as compared to performing the same process wherein the chemical compound is added at a concentration of below 7mM, wherein the chemical compound is selected from a list consisting of chemical structures with amino groups and/or cationic amino acid polymers, such as tetraethylene pentamine (TEPA), dipicolylamine (DPA), poly-lysine, poly-arginine and polyhistidine".

XIII. Claim 1 of auxiliary request 1 differs from claim 1 of the main request in that the claim is directed to a "[p]rocess for the purification of a polypeptide of interest by cation-exchange chromatography..." instead of to the "[u]se of a chemical compound for the reduction of host cell proteins in the purification of

a polypeptide of interest by cation-exchange chromatography...". Moreover, the chemical compound is defined as "selected from a list consisting of dipicolylamine (DPA), tetraethylene pentamine (TEPA), and cationic amino acid polymers, such as poly-lysine, poly-arginine and poly-histidine".

XIV. The submissions of appellant I (patent proprietor) are summarised as follows.

Main request - claim 1

Novelty (Article 54 EPC)

The claimed subject-matter was a (second) non-medical use of the type considered in decisions G 2/88, G 6/88, T 279/93 and T 892/94. As explained in G 2/88 Headnote 3:

"A claim to the use of a known compound **for a particular purpose, which is based on a technical effect which is described in the patent,** should be interpreted as including that technical effect as a functional technical feature, and is accordingly not open to objection under Article 54(1) EPC provided that such technical feature has not previously been made available to the public" (emphasis by the appellant).

The claim was precisely the type whose subject-matter should be recognised as novel under G 2/88 because it related to the use of a known compound for a new purpose not made available in the prior art – i.e. 'the reduction of host cell proteins (HCPs) in the purification of a polypeptide of interest by cation-exchange chromatography'. The latter part of the claim (following the word 'thereby') further specified the

specific effect of using the compound: i.e. that host cell proteins are reduced relative to the protein of interest, in the context of the process, by virtue of adding the compound of the claim.

The present case was therefore not one in which the patentee improperly sought to distinguish the claim over the prior art based on the rationale of G 2/88 merely by specifying 'the purpose of carrying out the process'. Rather, this was a case where the distinction came from the new purpose of using the compound, based on a technical effect described for the first time in the patent.

A number of decisions supported the view that the criteria set out in G 2/88 can be applied to claims like those in the main request, with claims whose wording meant that their subject-matter was the use of a known substance for a new purpose, based on a technical effect described in the patent, even though the new use was in the context of a process.

Decision T 149/22 concerned the 'use' of phospholipase A in cake production to reduce fat content. It held that the technical effect ("enable reduction of the amount of fat used in the recipe,") was a characterising feature and had to be considered for novelty.

Decision T 319/98 concerned "The use of one or more iodides of Group IA or Group IIA of the Periodic Table of the Elements or of hydrogen **for suppressing the volatility of water relative to acetic acid**.." (emphasis by appellant I). The functional feature (suppression of volatility) was considered a technical feature qualifying the invention.

In decision T 966/00 the board considered a claim directed to the use of specific polyethers to increase solubility of hydrocarbons, **in order to increase solubility of pure hydrocarbons in the polyol component** in the preparation of hard polyurethane foams. Here the increase in solubility was a novel technical effect not disclosed in the prior art.

Decision T 140/94 concerned the use of a protein to **inhibit formation of reddish colour** during heat processing of fruit/vegetable material. The technical effect (inhibition of colour formation) was not previously disclosed and thus conferred novelty.

T 332/94 the board decided on a claim for use of a lipolytic enzyme **as a spot-reducing agent** in a process for machine dishwashing or rinsing. It held that the prior art did not clearly and unambiguously disclose the enzyme's use for this specific purpose.

Further decisions cited were T 22/09, T 593/06.
It was clear from this line of case law that where a claim was directed to a second non-medical use novelty could be established by a specific technical effect.

In the present case that effect was reducing HCPs. This was a feature of the claimed use and had not been disclosed or suggested in the prior art. Thus, even if the same compounds had been used in prior processes, the purpose and effect claimed in former auxiliary request 4, now the main request, had not previously been made available to the public.

The new effect – i.e. competing for CEX binding and attaining the effect of reducing HCP impurities (as

compared to the same process wherein the chemical compound is added at a concentration of below 7mM) – was therefore to be treated as a functional technical feature of the claim and, provided the prior art did not make available the use of the known compound for the same purpose or effect, it imparted novelty to the claimed subject-matter.

Indeed, as explained in paragraphs 86-87 and 89-93 of the decision under appeal, for this claim to be anticipated in the prior art, a prior art document had to disclose the use of the same class of chemical compounds in the same method (CEX) for obtaining the same effect. A document merely disclosing the presence of the chemical compound in CEX but not relating the compound to reduction of HCPs, could not anticipate the claim. Rather, the prior art had to at least disclose a link between the chemical compound and the reduction of HCPs.

In conclusion, claim 1 was not a process claim but a second non-medical use claim. Therefore, the claimed subject-matter was novel over the cited prior art.

Turning to the cited prior art in more detail, document D2 disclosed the use of arginine in a loading fluid to solubilise the protein of interest and reduce aggregation. It taught that arginine binds to the protein of interest, not to the matrix (and thus did not even disclose a situation necessarily involving binding of arginine to the CEX matrix). Document D2 did not disclose that arginine was used for the purpose or effect of HCP removal. Thus, D2 failed to disclose the claimed new purpose and effect.

Document D4 disclosed the use of Tris buffer solutions, without any indication as to the particular function of Tris other than its use as a buffer (in line with its normal use in the art). In fact, Tris was mentioned in D4 at most as an optional buffer component. Therefore, it at most suggested the optional use of Tris for buffering, but not the use of Tris for reducing HCPs in CEX. There was therefore no indication that the CEX steps involve adjusting an equilibration fluid necessarily containing Tris (rather than Hepes), such that the Tris buffer component inevitably bound to the CEX matrix.

Document D5 failed to anticipate the claimed subject-matter because it fell far short of disclosing that a chemical compound according to the claims was used and that the use of the compound *per se* led to the reduction of HCPs.

Correction under Rule 139 EPC

The patent contained an error in the definition of the term "clustered". Paragraph [0082] in the patent as granted defined "clustered" as a non-even distribution of the negative charges, meaning that there is a local concentration of negative charges in the chemical compound. In the proceedings before the opposition division, it was requested that this be corrected to refer to "positive or negative charges", because the limitation to negative charges was an obvious error.

The opposition division refused the request because it considered that it is not immediately evident that an error occurred. However, this was not correct. The skilled reader would take account of the whole disclosure of the patent (or the application as filed)

in their assessment. It would have been immediately evident to them that an error occurred in paragraph [0082], and that the proposed correction was intended. When reading either patent or the application as filed, the skilled person would understand that the reference only to "negative charges" in this passage was an error because the application as filed explained that either compound polarity may have "clustered" charges (see page 15, lines 1-2 and claims 3, 16 and 22 of the application as filed). In addition, the patent and application as filed:

i) referred to compounds where the positive charge on the chemical compound is clustered (e.g. Patent [0046]),
ii) also referred to clustered charges on the polypeptide of interest, which may be positive or negative charges (Patent [0048], [0091]), and
iii) provided no alternative definition for "clustered" in the context of positive charges.

XV. The submissions of appellant II (opponent) are summarised as follows.

Main request - claim 1

Claim construction

Claim 1 drafted to the "use of a chemical compound for the reduction of host cell proteins in the purification of a polypeptide of interest by cation-exchange chromatography wherein the chemical compound was added in a concentration of at least 7 mM (…)". On the basis of decision T 892/94, the opposition division concluded that subject-matter of claim 1 was novel because the use of the chemical compound for the reduction of host

cell proteins was allegedly not disclosed in any of the cited documents.

However, even if the reduction of host cell proteins was not disclosed in any of the cited documents (which was disputed), the claimed subject-matter was not novel under the principles established in T 892/94.

In T 892/94 the board noted that according to G 2/88, novelty could be acknowledged for a claim directed to the use of a known substance for a hitherto unknown non-medical purpose reflecting a newly discovered technical effect. However, a newly discovered technical effect could not confer novelty on the use of a known substance for a known non-medical purpose if the newly discovered technical effect already underlay the known use of the known substance.

In the present case, the claimed non-medical purpose was purification of polypeptides using cation-exchange chromatography (CEX). This was not novel. The reduction of host cell proteins (HCP) was actually a technical effect of the old non-medical use, i.e. it was an explanation of a mechanism by which the purification was achieved and as such had to be disregarded as a feature of the claim.

Novelty (Article 54 EPC)

The chemical compound in the claim was to be selected from a list consisting of chemical structures with amino groups and/or cationic amino acid polymers, such as tetraethylene pentamine (TEPA), dipicolylamine (DPA), poly-lysine, poly-arginine and poly-histidine. Such a compound was known from any of documents D2, D4, D5 or D9.

Document D2 was an article on the effects of arginine on protein binding in ion exchange chromatography. In particular, CM-Sepharose was used, which was known as a weak CEX chromatography matrix and was also mentioned as an exemplary CEX matrix in paragraph [0083] of the opposed patent. Arginine was a chemical compound with an amino group. It was also a primary amine with an overall positive charge. D2 disclosed that the CM-Sepharose CEX column was equilibrated with 10 mM sodium acetate, pH 5.8 (page 111, left column, last paragraph). IL-6 was then loaded onto the column in the absence and presence of 0.2 M arginine in 20 mM sodium acetate. That means that in the process of D2, the loading fluid was adjusted such that at least part of the arginine was bound to the CEX matrix due to a charge that is opposite to the charge of the CEX matrix.

Furthermore, it could be seen from Figure 4 that using 0.2 M arginine decreased the amount of aggregates to less than 1% (page 113, paragraph bridging left and right columns). Therefore, D2 specifically disclosed the use of arginine in reducing impurities.

The decision under appeal mentioned in point 89 that D2 disclosed the use of arginine for the purpose of 'reducing aggregates' and implied that this was a different purpose than 'reduction of host cell proteins'. However, aggregates, and host cell proteins were all classified impurities. Thus, the reducing HCP was not a different purpose, but merely a sub-category of the known purpose.

Similarly, D4 disclosed the use of Tris and triethanolamine in CEX buffers, with high purity

achieved—implying impurity reduction. Also document D5 disclosed Tris in equilibration buffers used to remove protein impurities. Finally, D9 disclosed the use of urea in all CEX buffers to remove inclusion bodies (which included HCPs), thus teaching the same technical effect.

XVI. The final requests of the parties were as follows:

Appellant I requested that the decision under appeal be set aside and that the patent be maintained on the basis of the set of claims of the main request (former auxiliary request 4), or in the alternative on the basis of the claims of auxiliary request 1 (former auxiliary request 30 and renumbered as auxiliary request 24 with letter of 26 November 2024). Auxiliary requests 2 to 58 (corresponding to auxiliary requests 1 to 23 and 25 to 58 as renumbered with letter of 26 November 2024) were also maintained. It was furthermore requested that paragraph [0082] of the patent be corrected under Rule 139 EPC according to amended page 10 of the description, submitted on 18 June 2021.

Appellant II requested that the decision under appeal be set aside and that the patent be revoked in its entirety, except in the form of auxiliary request 1.

Reasons for the Decision

Main request - claim 1

Introduction

1. According to the patent (paragraph [0033]) the invention relates to "*processes for purifying*

polypeptides of interest from complex mixtures by increasing the amount of a polypeptide of interest bound to a cation-exchange matrix relative to the amount of one or more impurities bound to the ion-exchange matrix. This effect is achieved by adding a chemical compound in the process which by also binding to the ion-exchange matrix reduces the binding of impurities more than the binding of the polypeptide of interest. The complex mixtures above may result from recombinant production schemes or be e.g. human or animal body fluids, preferably blood or plasma solutions".

Claim construction

2. The parties do not agree on the category of the claim, i.e. whether the claimed subject-matter is a non-medical use in the sense of G 2/88 (OJ EPO 1990, 93) and G 6/88 (OJ EPO 1990, 114) or if it is a process for production of a product. As a consequence, they further disagree about whether the effect, defined in the claim as "reduction of host cell proteins" and also as "an increased ratio of the polypeptide of interest to host cell proteins in the eluate as compared to performing the same process" is a functional technical feature, limiting the claimed subject-matter or not.

3. In the decision under appeal, the opposition division took the view that the claim was "*clearly a (second) non-medical use claim*" (see point 85). In other words, it related to the use of a known compound for a particular purpose, based on a (new) technical effect. In the opposition division's view, the claim related to subject-matter falling under the rationale of decisions G 2/88 and G 6/88 of the Enlarged Board of Appeal, as further interpreted in decisions T 279/93 and T 892/94

and so "*a novelty anticipating document [had to] disclose the use of the same substance ("chemical compound") in the same method (CEX) for obtaining the same effect (reduction of HCPs). The underlying mechanism (in the present case binding of the chemical compound to the CEX matrix), whether being disclosed or not, whether being the same or another, [wa]s irrelevant*" (see point 86).

4. From the above it is clear that claim construction plays a key role in deciding on the novelty of the claimed subject-matter. That claim construction represents the first step in the assessment of novelty, in order to determine the technical features of the claimed subject-matter, was confirmed in decisions G 2/88, (Reasons 6) and G 6/88 (Reasons 8). The parties were also informed of this in the board's communication pursuant to Article 15(1) RPBA (see point 17).

5. When construing a claim in a patent, the claimed subject-matter is determined by applying the established principles of claim construction, i.e. giving the terms used in a claim their ordinary meaning in the context of the claim in which they appear (see T 681/01, reasons 2.1.1). This principle also applies when determining what "category" a claim is in, e.g. whether it is directed to a product or process.

6. These principles of claim construction were also applied in decisions G 2/88, in which the Enlarged Board had to decide whether a change of claim category by means of amendment gave rise to an extension of the scope of protection, in violation of Article 123(3) EPC, and in G 6/88. In relation to this, the Enlarged Board established that "*a claim to the use of a known compound for a particular purpose, which is based on a*

technical effect which is described in the patent, should be interpreted as including that technical effect as a functional technical feature, and is accordingly not open to objection under Article 54(1) EPC provided that such technical feature has not previously been made available to the public" (see G 2/88, Headnote III and G 6/88, Headnote). In other words, where a claimed invention involves a new technical effect of a known compound and the claimed subject-matter is the use of that known compound to achieve the new purpose based on the new effect, the subject-matter is novel even if the physical activity (the means of realisation) is identical to a physical activity known in the art (see G 2/88, Reasons 9.1).

7. It is furthermore apparent that in decision G 2/88, the Enlarged Board, as part of its considerations relating to Article 123(3) EPC (see point 5.1 of the Reasons), made a distinction between categories of claims, namely between those directed to a use of a physical entity for achieving an effect on the one hand and those directed to a process for the production of a product on the other. The Enlarged Board emphasised that a claim directed to the use of a known compound for a particular purpose is not a process claim within the meaning of Article 64(2) EPC. While a process claim extends its protection to "*the product directly obtained by such process*" by virtue of Article 64(2) EPC, a "use" claim of the type considered by the Enlarged Board does not result in a product and therefore no protection under Article 64(2) EPC arises. For this reason the Enlarged Board found that the change of category from a product claim to a use claim does not normally extend the scope of protection and is not in violation of Article 123(3) EPC. However an extension of scope is not excluded with a change into a

process claim. In this context it stated that "*...it could be considered that such a "use" claim is notionally equivalent to a claim to a "process including the step of using the compound", and that the effect of Article 64(2) EPC is to extend protection to the "product" of such process (whatever it is); thus there would be extension of protection within the meaning of Article 123(3) EPC by reason of the change from a claim to one physical entity (the compound) to a different physical entity (the "product" of the process of using the compound). In the Board's view, in relation to such a change of category to a "use" claim, Article 64(2) EPC does not normally have such an effect, however, for the following reason. Article 64(2) EPC is not directed to a patent whose claimed subject-matter is the use of a process to achieve an effect (this being the normal subject of a use claim): it is directed to a European patent whose claimed technical subject-matter is a* ***process of manufacture of a product;*** *the Article provides that for such a patent, protection is conferred not only upon the claimed process of manufacture, but also upon the product resulting directly from the manufacture.*

Thus, provided that a claim defines the use of a particular physical entity to achieve an "effect", and does not define such a use to produce a "product", the use claim is not a process claim within the meaning of Article 64(2) EPC" (emphasis added by the present board).

Thus, the Enlarged Board's findings relating to new uses of known compounds are limited to uses/methods/ processes which are not processes resulting in products, as referred to in Article 64(2) EPC. Moreover, claims which when correctly construed are

directed to processes resulting in products referred to in Article 64(2) EPC are not subject to the special treatment established under G 2/88 and G 6/88, even if they contain the word "use".

8. The board refers to recent decision T 1913/21, published after the oral proceedings in the present case, for an analysis of the relevant case law of the boards on second non-medical uses and with a focus on which claimed subject-matter was subject to the principles established by G 2/88 and G 6/88. The jurisprudence of the Boards starting from the Enlarged Board of Appeal's decisions was found to make a consistent and strict distinction made between claims directed to a 'use' of a known compound for achieving an effect, which does not result in a product and claims directed to a process leading to the production of a product (see reasons 10 to 14). The board concluded that there was "*a consistent line of jurisprudence, holding that the rationale of the Enlarged Board of Appeal's decisions G 2/88 and G 6/88 is limited to claims directed to (new) non-medical uses of a known compound for a particular purpose, and does not apply to processes for production within the meaning of Article 64(2) EPC. Furthermore, in order to be a limiting technical feature of the claim, the new purpose must relate to the use rather than to a property of the product. Thus, in the case of processes for producing a product, the "aim" of the process is not a functional feature of the claimed subject-matter even if it is explicitly recited in the claim. Novelty of the claimed subject-matter is assessed solely on the basis of the remaining features of the claimed process*" (Reasons 15).

9. Appellant I relied on decisions T 140/94, T 332/94, T 319/98, T 966/00, and T 593/06, T 22/09 and T 149/22 in which the claims were in the format of the use of a compound to achieve a particular effect and included method steps, which in its view, closely corresponded to present claim 1. It argued that in those cases, the competent board had interpreted the respective claim in the sense of G 2/88, meaning that the intended technical effect was considered to be a technical feature of the claimed subject-matter.

10. The board has the following observations of those cases.

11. In T 332/94 (see reasons 4), the invention related to "*Use of a lipolytic enzyme as a spot reducing agent in a process for machine dishwashing or rinsing..*". The Board, after examination of the cited prior art documents, reached the conclusion that the claimed use was novel, because the cited prior art documents did not disclose the use of lipolytic enzymes as spot reducing agents in a process for machine dishwashing or rinsing. Similarly, in T 22/09, the board held that in the case of a claim directed to "*Use of a modifying component for suppressing the solubility of a catalyst support in aqueous acid solutions and/or neutral aqueous solutions, when present in and/or on the catalyst support*", the purpose defined in the claim was a technical functional feature representing a technical effect, as established in G 2/88.

11.1 The present board considers that in decisions T 332/94 and T 22/09, the claimed 'use' when properly construed, was not a method for production that results in a product. As such, this board agrees that in these

decisions, the principles established in G 2/88 were correctly applied.

12. Decision T 140/94 (see reasons 6), concerned a claim which read as follows: "*Use of a protein to inhibit formation of a reddish colour during the heat processing treatment of a fruit or vegetable material containing leucoanthocyanidin red pigment precursors under conditions which are such as to induce the formation of a reddish colour in the fruit or vegetable material, the protein being added to the fruit or vegetable material to contact the leucoanthocyanidin red pigment precursors in an amount effective to inhibit formation of the reddish colour during the heat processing treatment.*"

12.1 On the subject of novelty, the board considered that the principles in G 2/88 applied and that the claimed subject-matter was novel because the cited prior art did not disclose the use of the known compound for the particular purpose recited in the claim.

13. In T 319/98 (see reasons 2.4 to 2.15), the board held that in the case of a claim directed to "*The use of one or more iodides of Group IA or Group IIA of the Periodic Table of the Elements or of hydrogen for suppressing the volatility of water relative to acetic acid in a process for the recovery of acetic acid from a composition comprising acetic acid and water..*", the functional feature stated in the claim was a technical feature of the invention in the sense of G 2/88. Thus, the principle laid down in point 9 of decision G 2/88, that "*in relation to a claim whose wording clearly defines a new use of a known compound, depending upon its particular wording in the context of the remainder of the patent, the proper interpretation of the claim*

will normally be such that the attaining of a new technical effect which underlies the new use is a technical feature of the claimed invention", applied.

14. In T 966/00, the board considered that in the case of a claim directed to the use of compounds to increase the solubility of pure hydrocarbons in the polyol component during the production of rigid polyurethane foams, the functional feature stated in the claim was a technical feature of the invention in the sense of G 2/88.

14.1 Decision T 593/06 concerned a claim for "*Use of a silicate compound ..... of the formula KuNavAlwCaxMgySiOz wherein K is potassium, Na is sodium, Al is aluminum, Ca is calcium, Mg is magnesium, Si is silica, and 0 is oxygen and u, v and w, independently range from about 0 to about 0.5; x in a method for preparing a glass composition*". The board simply stated that "*The subject matter of the claims in accordance with the auxiliary request relates to a second non-medical use*" (see point 1.2 of the reasons).

15. In T 149/22, the board held that for a claim directed to "*..use of a phospholipase A in the production of cake to enable reduction of the amount of fat used in the recipe, wherein the phospholipase is added during preparation of the batter and is allowed to act in-situ*", the effect "*reduction of the amount of fat used in the recipe*", was a characterising feature of claim 1 and had to be taken into account when assessing whether the subject-matter of this claim was novel over the prior art.

16. In contrast to the conclusions drawn in T 332/94 and T 22/09, the findings in T 140/94, T 319/98, T 966/00, T 593/06 and T 149/22 do not reflect the prevalent

established jurisprudence, as summarised above, in particular with regard to the fact that the effect recited in the claim must relate to the use, rather than to the product directly obtained by the process steps within the meaning of Article 64(2) EPC, in order to constitute a limiting feature in the sense of G 2/88. Importantly these decisions do not provide any reasoning as to why the claims were not regarded as claims directed to a process for the manufacture of a product, which would not allow the principles of G 2/88 to be applied, or conversely whether the competent boards were of the view that the principles of G 2/88 are transferable to process claims and why this should be so.

The claim

17. Claim 1 is directed to:

"Use of a chemical compound for the reduction of host cell proteins in the purification of a polypeptide of interest by cation-exchange chromatography wherein the chemical compound is added in a concentration of at least 7 mM".

17.1 The chemical compound is defined as "selected from a list consisting of chemical structures with amino groups and/or cationic amino acid polymers, such as tetraethylene pentamine (TEPA), dipicolylamine (DPA), poly-lysine, poly-arginine and polyhistidine". Thus, the compound to be used is any chemical compound with an amino group or any cationic amino acid polymer.

17.2 The aim or purpose of the use is defined as "the reduction of host cell proteins in the purification of a polypeptide of interest by cation-exchange

chromatography". The board notes that the use is therefore in the context of a method or process for purification of a polypeptide of interest by cation-exchange chromatography.

17.3 The claim also defines the product resulting from the purification process as having "an increased ratio of the polypeptide of interest to host cell proteins in the eluate as compared to performing the same process". Furthermore, the claimed use is defined as comprising the steps of adding the chemical compound in a concentration of at least 7 mM to one or more of three fluids used (the equilibration, loading and washing fluids) and within or as part of each of these steps it is further specified that each fluid is "adjusted such that at least part of the chemical compound in the equilibration fluid binds to the cation-exchange matrix due to a charge that is opposite to the charge of the cation-exchange matrix". The chemical compound must therefore be present as a cation, so as to be able to bind to the cation exchange material. The claim does not give any detail on how the adjustment is to be done, although the description at paragraph [0070] states that "*In the sense of the invention "adjust" means the setting of the operating parameters at a specific step of the IEX [ion exchange]. This includes adjusting a certain pH, a certain conductivity, a certain temperature, a certain flow rate and the adjustment of other parameters of an IEX know[n] by the man skilled in the art. The parameters are set such that at least part of the chemical compound in the equilibration fluid and/or the loading fluid and/or the washing fluid binds to the ion exchange matrix*." It is apparent that at least some of these parameters, e.g. adjusting the flow rate, are process steps, which further confirms the board's view that the claimed

'use' in fact consists of the process of actually carrying out the ion-exchange chromatography.

17.4 Finally, the claim includes a mechanistic explanation of the effect achieved by carrying out a CEX purification using the fluid defined in parts a) to c) of the claim, "thereby increasing the amount of the polypeptide of interest bound to the cation-exchange matrix relative to the amount of host cell proteins bound to the cation-exchange matrix before the cation exchange matrix is eluted".

18. Considering the above, it is apparent that the purpose or aim defined in the claim can only be achieved in the context of a method or process for purification of a polypeptide of interest by cation-exchange chromatography. In fact, the claimed use includes carrying out explicitly defined process steps including the cation exchange chromatography steps of equilibrating, loading, and washing/eluting a CEX material using the fluids defined in the claim, leading to an eluate. Moreover, the aim "the reduction of host cell proteins" can only be achieved if the entire purification process is actually carried out and most importantly, the technical effect relied on is a property of the final product, i.e. an eluate containing an increased ratio of the polypeptide of interest to host cell proteins as compared to an eluate obtained when performing the same process wherein the chemical compound is added at a concentration of below 7mM,the purified polypeptide.

19. Thus, following the principles laid down in G 2/88 and G 6/88 and the jurisprudence implementing them, the board concludes that the claimed subject-matter must be regarded as a process for the purification of a

polypeptide of interest, in other words as a method for the production of an eluate with "an increased ratio of the polypeptide of interest to host cell proteins in the eluate as compared to performing the same process wherein the chemical compound is added at a concentration of below 7mM". As noted above, the technical effect "reduction of host cell proteins" cannot occur except as part of a process leading to the production of a product, here purified polypeptides, and as such is inextricably linked to the production process.

20. The board considers that the purified polypeptides produced by the claimed process would be covered by Article 64(2) EPC as "products directly obtained" by the claimed process. The board concurs in this regard with the findings in T 892/94 (Reasons 3.8) that applying the concept of novelty developed in G 2/88 to claims for processes of producing a product, even when drafted as use for achieving a technical effect that results in an improved product could potentially result in a permanent monopoly of the use of a known substance for a known purpose. Such a permanent monopoly would arise from the repeated drafting of claims for a process of production including a new, possibly only subtly different, technical effect associated with this known process (see also T 1179/07, Reasons 2.1.3).

21. In the present case, drafting the claim as a "use" of a chemical compound cannot mask the fact that the claim defines a production/purification process and the new technical effect can only take place in the context of this process. The mere formatting of the claim to give the appearance that its subject-matter falls under the principles established by G 2/88 cannot circumvent the fact that on analysis, the claim is directed to a use

or process for the production of a product, here one having the 'improved' property of having 'reduction of host cell proteins'.

22. Moreover, the alleged new technical effect of reduction of host cell proteins pertains to the product (the polypeptide) and cannot be considered a technical limiting feature of the 'use' according to G 2/88. Indeed, where an invention relates to a new technical effect of a physical entity that can only occur as part of a process for the production or manufacture of a product, such that this effect is inextricably linked to and cannot occur in isolation from the production process, a claim directed to that 'use' of the physical entity to achieve that effect must be regarded as directed to the production process *per se* (cf. T 1913/21, headnote 3).

Novelty (Article 54 EPC)

23. The assessment of novelty in the present case will therefore be done by answering the question of whether or not there was a disclosure forming part of the state of the art of a process having the same physical steps as the claimed process, i.e. purifying a polypeptide of interest by CEX chromatography, wherein at least one of the equilibration, loading and/or washing fluids contains a chemical structure with amino groups and/or cationic amino acid polymers, in a concentration of at least 7 mM. No other features are explicitly or implicitly implied by the wording of the claim.

24. On appeal, appellant II maintained an objection of lack of novelty of the subject-matter of claim 1 of the main request in view of documents D2, D4, D5 and D9. In its

view, if any of these documents discloses a process as claimed, the main request will not be allowable.

25. Appellant I's main line of argument in response to these objections (see reply to appellant II's statement of grounds of appeal and the letter dated 11 April 2023) was that "*The new effect – i.e. competing for CEX binding and attaining the effect of reducing HCP impurities (as compared to the same process wherein the chemical compound is added at a concentration of below 7mM) – is therefore treated as a functional technical feature of the claim and, provided the prior art does not make available the use of the known compound for the same purpose or effect, the claim is novel.*

Indeed, as explained in paragraphs 86-87 and 89-93 of the OD's decision, for this claim to be anticipated in the prior art, a prior art document must disclose the use of the same class of chemical compounds in the same method (CEX) for obtaining the same effect. A document merely disclosing the presence of the chemical compound in CEX but not relating the compound to reduction of HCPs, cannot be considered to anticipate the claim. Rather, the prior art must at least disclose a link between the chemical compound and the reduction of HCPs. However, none of the cited prior art documents do so" (see letter of 11 April 2023, paragraphs 5.8 and 5.9).

26. This argument cannot succeed because the board does not agree with appellant I's construction of the claim (see points 2. to 22. above). In view of the board's claim construction, the effect mentioned in the claim (i.e increasing the ratio of the polypeptide of interest to host cell proteins in the eluate) is not a feature of

the claimed process to be taken into account for assessing novelty.

Document D2

27. As set out in the decision under appeal (point 34), D2 discloses (CM-sepharose) CEX chromatography of proteins of interest. In one experiment of purifying IgG-4A antibodies the loading buffer comprised >7mM arginine and had a pH of 4 (see Table 1). D2 also reports a "*previous observation*", where IL-6 was purified the column was equilibrated at pH 5.8 (page 111, left-hand column, last three lines). IL-6 was then loaded onto the column in the absence and presence of 0.2 M arginine in 20 mM sodium acetate. Arginine was therefore protonated and present as a positively charged amine as required by the claim.

28. Thus, document D2 discloses a process for the purification of a polypeptide by means of CEX chromatography wherein arginine (a chemical compound falling with the definition provided in the claim) is added to both loading and elution fluids. The disclosure in document D2 anticipates the presently claimed subject-matter.

29. For this reason alone the main request is not allowable.

Document D4

30. As set out in the decision under appeal (point 36), document D4 discloses the purification of Apo-2 ligand proteins by CEX. In Example 10 it is disclosed that Tris is present in the loading fluid, equilibration fluid and washing fluid. At this pH, Tris is present in

its protonated form. Since Tris is a chemical compound falling with the definition provided in the claim, the CEX method disclosed in document D4 anticipates the subject-matter of claim 1.

Document D5

31. Document D5 also relates to the Apo-2 ligand and also discloses a purification process including a CEX chromatography step. In Example 2 conditioned, clarified cell lysate was loaded onto a cation exchange column, equilibrated in 50 mM Hepes (or 50 mM Tris)/ 0.05% Triton-X 100/1 mM DTT, pH 7.5 column. This disclosure anticipates the claimed subject-matter for the same reasons as given for document D4.

Document D9

32. Appellant II also considered that document D9 anticipated the claimed subject-matter, in contradiction to the opposition division's finding in points 45 and 46 of the decision under appeal. In view of the board's decision on novelty with respect to the disclosure in document D2, D4 and D5, novelty with respect D9 need not be decided.

33. In view of the above considerations, the set of claims of the main request is not allowable.

Auxiliary request 1

34. This claim request was former auxiliary request 30 and renumbered as auxiliary request 24 with letter of 26 November 2024. It was promoted to be auxiliary

request 1 during the oral proceedings before the board. Appellant II (opponent) had no objections against this claim request, either in relation to its admittance or on the merits.

35. The subject-matter of claim 1 is a process for the purification of a polypeptide of interest by cation-exchange chromatography wherein a chemical compound is added to the equilibration, loading and/or washing fluid in a concentration of at least 7 mM. Claim 1 overcomes the issue of lack of novelty found by the opposition division for the subject-matter of the main request before it, by limitation of the identity of the chemical compound to be added to the equilibration, loading and/or washing fluids.

36. Appellant II has no objections to this claim request. Moreover, its subject-matter overcomes the novelty objections that led to the opposition division's finding of lack of novelty with respect to claim 1 of the then main request, which were based on documents D2 to D6 and D10. These documents all disclose the purification of polypeptides by CEX, but none of them disclose that any of dipicolylamine (DPA), tetraethylene pentamine (TEPA), and cationic amino acid polymers, such as poly-lysine, poly-arginine and poly-histidine are added to any of the equilibration, loading and/or washing fluids in a concentration of at least 7 mM.

37. The board has no objections of its own motion under any other provisions of the EPC.

38. Thus, auxiliary request 1 is allowable.

Request for correction under Rule 139 EPC

39. Appellant I requested the correction of paragraph [0082] of the patent. The board decided not to allow this request. If the request for correction of linguistic errors, errors of transcription and mistakes in any document filed with the EPO concerns the description, claims or drawings, in order for the correction to be allowable under Rule 139 EPC, it must be established that (i) it is obvious that an error is in fact present in the document filed with the EPO, the incorrect information having to be objectively recognisable by the skilled person using common general knowledge, and (ii) the correction must be obvious in the sense that it is immediately evident that nothing else would have been intended than what is offered as the correction (see e.g. T 1626/16, Reasons 1.3).

40. In the present case, the board considers that at least the first of these requirements is not fulfilled. Paragraph [0082] of the patent reads "*In the sense of the invention the term "clustered" means a non-even distribution of the negative charges, meaning that there is a local concentration of negative charges in the chemical compound*". As already pointed out in the decision under appeal, there is nothing in the paragraph that would cause the skilled person to consider that an error had occurred. Since the content of the paragraph is not technically meaningless or self contradictory, it is entirely conceivable that this was the exact intention of the author, even if an additional option (a non-even distribution of the positive charges) would also be technically meaningful.

41. The request for correction under Rule 139 is rejected.

42. In view of the above conclusion, it is not necessary to consider whether Rule 139 EPC is available in opposition/opposition appeal proceedings

Order

For these reasons it is decided that:

1. The appealed decision is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent on the following basis:
- claims 1 and 2 of auxiliary request 1, which was former auxiliary request 30 and renumbered as auxiliary request 24 with letter of 26 November 2024,
- description and drawings possibly to be adapted thereto.

The Registrar: The Chairwoman:

I. Aperribay M. Pregetter

Decision electronically authenticated