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Case Number: T 2450/22 - 3.3.08

Application Number: 16188552.0

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Language of the proceedings: EN

Title of invention:
Method for the expression of polypeptides using modified nucleic acids

Patent Proprietor:
F. Hoffmann-La Roche AG

Opponent:
Scorpio IP Limited

Headword:
Expression of polypeptides/HOFFMANN-LA ROCHE

Relevant legal provisions:
EPC Art. 123(3)

Keyword:
Extension of protection conferred (yes)

Decisions cited:
G 0001/93, T 0190/99

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Case Number: T 2450/22 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 14 March 2024

Appellant: (Patent Proprietor)	F. Hoffmann-La Roche AG Grenzacherstrasse 124 4070 Basel (CH)
Representative:	Vossius & Partner Patentanwälte Rechtsanwälte mbB P.O. Box 86 07 67 81634 München (DE)
Respondent: (Opponent)	Scorpio IP Limited Mercury House 19-21 Chapel Street Marlow Buckinghamshire SL7 3HN (GB)
Representative:	Sagittarius IP Marlow International Parkway Marlow, SL7 1YL (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 5 September 2022 concerning maintenance of the European Patent No. 3138917 in amended form**

Composition of the Board:

Chair	R. Morawetz
Members:	B. Claes
	D. Prietzel-Funk

Summary of Facts and Submissions

I. The appeal lodged by the patent proprietor (appellant) lies from the interlocutory decision of the opposition division that European patent No. 3 138 917 entitled "*Method for the expression of polypeptides using modified nucleic acids*", with the set of claims of auxiliary request 1 filed at the oral proceedings, and the invention to which it relates meet the requirements of the EPC. The patent was granted for European patent application No. 16188552.0 (divisional application as filed), a divisional application of the earlier European patent application No. 13718536.9.

Claim 1 as granted reads as follows:

"1. A method for recombinantly producing a polypeptide in a CHO cell, comprising the step of cultivating a CHO cell which comprises a nucleic acid encoding the polypeptide, and recovering the polypeptide from the CHO cell or the cultivation medium,

wherein each of the amino acid residues of the polypeptide is encoded by at least one codon, whereby the codon(s) encoding the same amino acid residue are combined in one group and each of the codons in a group is defined by a specific usage frequency within the group, which is the frequency with which a single codon of a group of codons can be found in a nucleic acid encoding a polypeptide in relation to all codons of one group, whereby the sum of the specific usage frequencies of all codons in one group is 100 %, wherein the overall usage frequency of each codon in the genome of the cell is about the same as its specific usage frequency within its group,

wherein the usage frequency of a codon in the polypeptide encoding nucleic acid is about the same as its specific usage frequency within its group,

wherein the amino acid codon motif for
alanine is selected from SEQ ID NO: 64, 65, 66, 67 and 68, and/or
arginine is selected from SEQ ID NO: 69 and 70, and/or
asparagine is selected from SEQ ID NO: 71 and 72, and/or
aspartic acid is selected from SEQ ID NO: 73 and 74, and/or,
cysteine is selected from SEQ ID NO: 75 and 76, and/or
glutamine is selected from SEQ ID NO: 77, 78, 79, and 80, and/or
glutamic acid is selected from SEQ ID NO: 81 and 82, and/or
glycine is selected from SEQ ID NO: 83 and 84, and/or
histidine is selected from SEQ ID NO: 85 and 86, and/or
isoleucine is selected from SEQ ID NO: 87 and 88, and/or
leucine is selected from SEQ ID NO: 89, 90 and 91, and/or
lysine is selected from SEQ ID NO: 92 and 93, and/or
phenylalanine is selected from SEQ ID NO: 94 and 95, and/or
proline is selected from SEQ ID NO: 96 and 97, and/or
serine is selected from, SEQ ID NO: 98, 99 and 100, and/or
threonine is selected from SEQ ID NO: 101, 102 and 103, and/or
tyrosine is selected from SEQ ID NO: 104 and 105, and/or
valine is selected from SEQ ID NO: 106, 107 and 108."

II. The opposition division decided that claim 1 of the main request (filed with the submission of 16 March 2022) extended the protection conferred by the patent (Article 123(3) EPC).

Sole independent claim 1 of the main request - the set of claims being identical to the main request of the appeal proceedings - reads, with emphasis added by the board as compared to sole independent claim 1 of the patent as granted (strike-through: deleted; underlined: added) and denomination of features in bold in brackets:

"1. A method for recombinantly producing a polypeptide in a CHO cell, comprising the step of cultivating a CHO cell which comprises a nucleic acid encoding the polypeptide, and recovering the polypeptide from the CHO cell or the cultivation medium,
(features (i) to (iii))

wherein each of the amino acid residues of the polypeptide is encoded by at least one codon **(feature (iv))**, whereby the codon(s) encoding the same amino acid residue are combined in one group and each of the codons in a group is defined by a specific usage frequency within the group **(feature (v))**, which is the frequency with which a single codon of a group of codons can be found in ~~a~~ the nucleic acid encoding ~~a~~ the polypeptide in relation to all codons of one group **(feature (vi))**, whereby the sum of the specific usage frequencies of all codons in one group is 100 % **(feature (vii))**, wherein the overall usage frequency of each codon in the genome of the cell is about the same as its specific usa~~ge frequency within its group,~~
(feature (viii))

~~wherein the usage frequency of a codon in the polypeptide encoding nucleic acid is about the same as its specific usage frequency within its group,~~
(feature (ix))

wherein the amino acid codon motif for

alanine is selected from SEQ ID NO: 64, 65, 66, 67 and 68, and~~/or~~
arginine is selected from SEQ ID NO: 69 and 70, and~~/or~~
asparagine is selected from SEQ ID NO: 71 and 72, and~~/or~~
aspartic acid is selected from SEQ ID NO: 73 and 74, and~~/or~~
cysteine is selected from SEQ ID NO: 75 and 76, and~~/or~~
glutamine is selected from SEQ ID NO: 77, 78, 79, and 80, and~~/or~~
glutamic acid is selected from SEQ ID NO: 81 and 82, and~~/or~~
glycine is selected from SEQ ID NO: 83 and 84, and~~/or~~
histidine is selected from SEQ ID NO: 85 and 86, and~~/or~~
isoleucine is selected from SEQ ID NO: 87 and 88, and~~/or~~
leucine is selected from SEQ ID NO: 89, 90 and 91, and~~/or~~
lysine is selected from SEQ ID NO: 92 and 93, and~~/or~~
phenylalanine is selected from SEQ ID NO: 94 and 95, and~~/or~~
proline is selected from SEQ ID NO: 96 and 97, and~~/or~~
serine is selected from, SEQ ID NO: 98, 99 and 100, and ~~/or~~
threonine is selected from SEQ ID NO: 101, 102 and 103, and~~/or~~
tyrosine is selected from SEQ ID NO: 104 and 105, and~~/or~~

valine is selected from SEQ ID NO: 106, 107 and 108; **(feature (x))**

wherein for each sequential occurrence of a specific amino acid in the polypeptide starting from the N-terminus of the polypeptide, the encoding nucleic acid comprises the codon that is the same as that at the corresponding sequential position in the amino acid codon motif **(feature (xi))**; and
wherein after the final codon of the amino acid codon motif at the next occurrence of the specific amino acid in the polypeptide the encoding nucleic acid comprises the codon that is at the first position of the amino acid codon motif." **(feature (xii))**

III. After the parties were summoned to oral proceedings, the board issued a communication under Article 15(1) RPBA in which it concurred with the opposition division that claim 1 of the main request extended the protection conferred by the patent as granted (Article 123(3) EPC).

IV. The relevant submissions and arguments of the parties in appeal are reflected in the reasons for the decision below.

V. At the end of the oral proceedings and after the appellant had withdrawn two auxiliary requests, the parties' requests were as follows.

The appellant requested that the decision under appeal be set aside and the patent be maintained in amended form on the basis of the main request filed with the statement setting out the grounds of appeal.

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

Reasons for the Decision

The invention claimed in the granted patent

1. The board agrees with the appellant that the gist of the invention disclosed in the patent is a method for codon optimisation in polypeptide-encoding nucleic acid sequences by mirroring, in a practically applicable manner, CHO cell (overall) genomic codon frequencies (see table in paragraph [0176] of the patent) to optimise the polypeptide's expression in the recombinant CHO host cell system. To this end, paragraphs [0177] to [0243] of the patent disclose the derivation and design of particular amino acid codon motifs representing a practical and manageable approximation of the codon usage frequency for each amino acid in CHO cells for use in the design of coding sequences for optimal expression in the CHO expression system.

2. The use of amino acid codon motifs for designing recombinant coding sequences for expressing and recovering polypeptides in CHO cells is based on the overall codon usage frequency occurring in CHO cells (see table in paragraph [0176] of the patent), and the usage frequency of each codon in the respective groups of codons encoding one (i.e. the same) amino acid residue is defined (see, for example, for the amino acid alanine (Ala), paragraphs [0177] to [0185] of the patent). The amino acid codon motifs thus provide conceptual design instructions for the distribution of the various codons in a polypeptide-encoding nucleic

acid when optimised for expression in CHO cells. The codon optimisation method disclosed in the patent accordingly does not require codon optimisation to a level at which the codon usage frequencies in a given designed nucleic acid encoding a polypeptide approach, with mathematical precision, the overall CHO cell genomic codon usage frequencies.

3. Sole independent claim 1 of the patent as granted (see section I.) relates to a method of codon optimisation in which codons in a polypeptide-encoding nucleic acid sequence are selected - both in terms of codon type and codon order - to optimise polypeptide expression in a recombinant CHO host cell system, a common mammalian system for the mass production of recombinant proteins.

4. Feature (ix) in claim 1 as granted requires that "the usage frequency of a codon in the polypeptide encoding nucleic acid is about the same as its specific usage frequency within its group"; a "group" of codons being the (different) codons encoding the same amino acid (degeneracy of the genetic code (see feature (v) of claim 1)).

5. Feature (x) in the claim recites amino acid codon motifs for each amino acid which provide the order of usage of codons encoding a given amino acid in the polypeptide to be expressed. The amino acid codon motifs are presented as SEQ ID NOs, which correspond to nucleic acid sequences. Granted claim 1 refers to 45 codon motifs corresponding to the 18 natural amino acids which according to the genetic code are encoded by more than one codon.

Main request - claim 1
Extension of the scope of protection (Article 123(3) EPC)

6. The aim of Article 123(3) EPC is to protect the interests of third parties by prohibiting any broadening of the claims of a granted patent, even if there should be a basis for such broadening in the application as filed (see decision G 1/93, OJ EPO, 1994, 541). In accordance with the general intention of Article 123(3) EPC, there should be legal certainty for third parties that the protection conferred by a patent can only be restricted, not extended. The object of Article 123(3) EPC is thus to prevent situations where an act that did not infringe the patent as granted becomes an infringing act due to an amendment made after grant (see Case Law of the Boards of Appeal, 10th edn., 2022 (CLBA), II.E.2.1 and the decisions cited there).

The decision under appeal

7. The opposition division decided that the deletion of the feature "*wherein the usage frequency of a codon in the polypeptide encoding nucleic acid is about the same as its specific usage frequency within its group*" (feature (ix), see section II.) from the wording of granted claim 1 constituted an amendment which extended the protection conferred by the patent.

8. In essence, the opposition division dismissed the argument of the patent proprietor that amended feature (x) in claim 1 of the main request, which now required the use of a specified motif for codon optimisation for *each and every* amino acid mentioned (amendment from the "and/or" operators in granted claim 1 to the "and" operator in claim 1 of the main request), necessarily provided compliance with the technical requirements of deleted feature (ix) (i.e.

led to a usage frequency of a codon in the polypeptide-encoding nucleic acid which was *about the same* as its usage frequency within its group), so that, contrary to what was argued by the opposition division, deletion of feature (ix) did not lead to an extension of the scope of protection compared to granted claim 1.

9. The opposition division supported this conclusion with an example of an embodiment that infringed claim 1 of the main request but not the patent as granted. In that example, SEQ ID NO: 64 (corresponding to the codon motif "gcc gcc gcc gcc gct gct gct gca gca gcg") was chosen for codon optimisation of the operand for the amino acid alanine ("Ala", selected from the applicable operand "*wherein the amino acid codon motif for alanine is selected from SEQ ID NO: 64, 65, 66, 67 and 68*" in granted claim 1, see section I.) in the claimed method as granted. In accordance with feature (x), the specific codon usage frequency within this group was 40% for the gcc codon (used four times in the motif), 30% for the gct codon (used three times in the motif), 20% for the gca codon (used twice in the motif) and 10% for the gcg codon (used once in the motif), thus arguably in accordance with the disclosure of the invention in the patent and complying with the requirements of features (viii) and (ix) in granted claim 1.

10. However, if the same motif was used for codon optimisation to express and recover a polypeptide that contains fewer than ten Ala residues (the total number of codons in the motif) or a multiple of that number, the proportion of codons in the nucleic acid encoding the polypeptide would no longer be the same or about the same as in the corresponding group as required by

feature (ix) in granted claim 1.

11. For instance, applying the method of claim 1 of the main request to a polypeptide comprising only five Ala residues using the codon motif in SEQ ID NO: 64, resulted for Ala in a codon usage frequency of 80% gcc (first four codons in the motif used for the first to fourth occurrence of Ala) and 20% gct (fifth codon in the motif used for the fifth occurrence of Ala), thus substantially different (beyond being "about the same") from the codon usage frequencies of 40% for the gcc codon and 30% for the gct codon within the group and required by feature (ix) in granted claim 1 (see point 9. above). A similar situation arose when a polypeptide with 15 Ala residues was produced by the method of claim 1 of the main request. Here, applying feature (x) of the claimed method resulted in a codon usage frequency of 53.3% for the gcc codon, 26.6% for the gct codon, 13.3% for the gca codon and 6.6% for the gcg codon, or, rounded, 50% for the gcc codon, 30% for the gct codon, 10% for the gca codon and 10% for the gcg codon, thus again substantially different (beyond being "about the same") from the codon usage frequencies within the group.

12. The opposition division concluded that the use of nucleic acids with the Ala codon usage frequency referred to in point 11. were *excluded* from granted claim 1 by feature (ix) but were now encompassed by claim 1 of the main request. Indeed, a codon usage frequency of e.g. 80% (in the case of the gcc codon for expressing a polypeptide comprising five Ala residues) would have been excluded from granted claim 1 by feature (ix) since 80% was not "about the same" as the codon usage frequency of 40% within the group of codons used as the reference in feature (ix).

13. The opposition division thus decided that the absence of feature (ix) in claim 1 of the main request extended the scope of protection compared to that provided by granted claim 1 and, therefore, infringed Article 123(3) EPC.

Appellant's appeal case

14. On appeal, the appellant reiterated and expanded on the arguments that the opposition division had dismissed (see point 8.) and objected to the opposition division's calculations and conclusions.

15. The essence of the appellant's first line of argument was that feature (x) of claim 1 of the main request represented a particularly preferred *embodiment* and an implementation of the codon optimisation rules spelt out in features (iv) to (ix) in granted claim 1 which could hence be deleted without broadening the protection provided.

15.1 Features (viii) and (ix) in granted claim 1 using the wording "about the same as its specific usage frequency within its group" for the overall usage frequency of each codon in the cell's genome and the usage frequency of a codon in the polypeptide-encoding nucleic acid used for expression, respectively, captured the essence of the approximation of the invention set out in features (iv) to (ix). At the same time, feature (x) reflected the core of the disclosed invention (see paragraphs [0176] to [0242] of the patent) as the motifs were the concrete implementation of the derivation rules spelt out in features (iv) to (ix) and thus also of the "about the same" rule in feature (ix). Therefore, applying the codon optimisation of features

(iv) to (ix) of granted claim 1 resulted in *the same kind* of polypeptide-encoding sequence as when applying the optimisation of the group of features (x) to (xii) in claim 1 of the main request based on codon motifs. This group of features was thus consistent, and fulfilment of the group of features (x) to (xii) in claim 1 of the main request meant that deleted feature (ix) was also complied with.

15.2 Because feature (x) in granted claim 1 directly followed feature (ix), the mandatory codon definition for each amino acid residue in feature (x) of claim 1 of the main request was the logical implementation of all preceding features in granted claim 1, including feature (ix). Although, due to the "and/or" conjunction between the SEQ ID NOs for a given amino acid in feature (x) in granted claim 1, only at least one amino acid was encoded according to a motif. Nevertheless, *each* selection of a codon motif for an amino acid necessarily satisfied feature (ix). The subject-matter of claim 1 of the main request (deletion of "/or" from the operator "and/or") constituted a particularly preferred embodiment encompassed by claim 1 as granted. Therefore, with the incorporation of features (x) to (xii) and the further limitation of the operands by the "and" operator alternative in claim 1 of the main request, feature (ix) became obsolete in the claim as the codon motifs defined the frequency feature (ix) and, furthermore, provided additional sequence limitations. Deleting feature (ix) as done in claim 1 of the main request could thus not extend the protection provided by the amended claim in the presence of features (x) to (xii).

15.3 The necessity for feature (x) to satisfy feature (ix) in claim 1 as granted could also be derived from the

claims filed with the (divisional) application. While claim 1 as filed contained features (i) to (v), (vii) and (ix) of granted claim 1, the motif definitions of feature (x) were the subject of dependent claim 11 as filed. Hence, claim 11 as filed incorporated all the features of claim 1, and feature (x) in claim 11 as filed therefore constituted an embodiment of claim 1 as filed.

15.4 In the notice of opposition, the respondent construed granted claim 1 such that a polypeptide fell under its scope "*(i) if at least for one amino acid present in the polypeptide a codon motif is used to select the codons; and (ii) - in case the amino acid is present at a number below the number of codons in the motif - if the codons encoding said amino acid correspond only to part of the motif (i.e., the amino acid is present in the polypeptide at a number that is below the number of codons in a motif provided in the claim for the respective amino acid, including the occurrence of one residue)*" (appellant's letter dated 12 January 2024, item 1.3).

16. Claim 1 as granted is for a method for recombinantly producing and recovering a polypeptide based on a nucleic acid in which the coding region is designed in accordance with the provisions in features (iv) to (viii), (ix) and (x) (see section I.). Each of these design provisions in claim 1 has a different wording and technical meaning and provides *different* limitations to the codon usage for designing the nucleic acid sequence. While features (iv) to (viii) and (ix) relate to and limit the codon usage frequency in the design of the polypeptide-encoding nucleic acid sequence, feature (x) provides different rules for the

codon usage frequency and, in addition, rules for the order of use of the codons.

17. First, the board is unable to identify any indication in the wording of claim 1 as granted that compliance with the limitations of one provision on the codon usage frequency in the design of the codon sequence necessarily provides compliance with another provision. Given the wording of granted claim 1, the fact that feature (x) directly follows feature (ix) cannot provide such an indication seeing that the same subject-matter would be considered to result from a claim with feature (ix) following feature (x).

18. Second, the board cannot identify in the wording of claim 1 as granted any indication that the usage of any given codon motif listed in feature (x) for designing the polypeptide-encoding nucleic acid sequence necessarily results in a nucleic acid sequence that complies with feature (ix). In fact, no indication for such a guarantee can be derived from the patent, either.

19. Third, the board agrees with the respondent that the fact that the divisional application was filed with a set of claims with claim 1 containing features (i) to (v), (vii) and (ix) of granted claim 1 and claim 11 dependent on it with feature (x) of granted claim 1 does not mean that every embodiment of feature (x) must be covered by the independent claim. In any case, the filed set of claims cannot go beyond providing an insight into the intentions of the applicant for the dependent claim in the divisional application. It cannot provide guidance for interpreting the scope of protection provided by a set of claims where such a dependent claim is no longer present. The appellant's

arguments that rely on the set of claims filed with the application must therefore also fail.

20. The board concludes, contrary to the appellant's submissions, that neither the claims nor the patent provides for an exclusive application of feature (ix) to the usage frequency of those amino acids referred to in claim 1 as granted which are not optimised using a specified motif depicted in the SEQ ID NOs. In fact, the restrictions of feature (ix) in claim 1 as granted also have a limiting effect on the codon usage of those amino acids referred to in granted claim 1 which are chosen to be optimised in the claimed method. The board is accordingly not persuaded by the appellant's line of argument that feature (x) of the main request - in which for each given amino acid a particular codon motif is necessarily selected from those listed - represented a particularly preferred embodiment of features (iv) to (ix) in granted claim 1.

21. For the sake of completeness, the board notes that points 3.4 to 3.9 of the notice of opposition, to which the appellant referred (see point15.4 above), concern the construction of feature (x) rather than granted claim 1 as a whole (see point 3.5: "[t]*his means that integer (x) is satisfied if ...*"; and points 3.7 and 3.9: "[w]*e construe the language of claim 1 to mean that, ... integer (x) is satisfied if ...*"). Feature (ix) of granted claim is not mentioned. Accordingly, for this reason alone, the appellant's argument is not persuasive.

22. The appellant's second line of argument related to the results of the opposition division's calculations demonstrating that the absence of feature (ix) in claim 1 of the main request extended the scope of

protection as compared to that provided by granted claim 1 (see points 9. to 12., above). It was argued that, also having regard to feature (ix), granted claim 1 actually *allowed* for the use of nucleic acids with an Ala codon usage frequency calculated by the opposition division and referred to in point 11. above.

22.1 The illustrative example chosen by the opposition division did not correspond to a "real world" situation of a polypeptide intended to be expressed and recovered in accordance with claim 1 as granted and of the main request. The calculations for the Ala amino acid (see points 9. to 12.) were artificial and deliberately extreme. The claims should be read with a mind willing to understand given that the invention in the patent aimed at a codon usage frequency approximation (see point15.1), not mathematical precision. In fact, if the opposition division's calculations were pertinent, the method of claim 1 as granted would only be applicable to polypeptides where the number of residues of the amino acids with codon degeneracy corresponded to the number of codons in the respective motifs or multiples of this number. The claimed method was, however, not so restricted and in fact applicable to any polypeptide for expression in CHO cells, and the patent did not disclose anything to the contrary.

22.2 The examples of the patent confirmed that considerable deviations in the codon frequency between the group (feature (ix)) and the polypeptide-encoding nucleic acid in accordance with feature (x) was possible. Indeed, the test polypeptide having the sequence SEQ ID NO: 57 (see paragraph [0158] of the patent) expressed in the examples of the patent contained only one cysteine residue (position 259). In the optimised nucleotide sequence encoding the test polypeptide with

SEQ ID NO: 63 (see paragraph [0162] and table in paragraph [0164] of the patent), the tgc codon was thus used for the cysteine residue, i.e. the codon first mentioned in each of the cysteine amino acid codon motifs in the operand for cysteine in feature (x) (SEQ ID NOs: 15 to 17). This resulted in a codon frequency of 100% for the tgc codon in the coding sequence, although the relative frequency of this codon in the cysteine group was only 64% (see table on page 24 of the patent, right-hand column, bottom row) and the amino acid codon motifs for cysteine for use in *E. coli* (SEQ ID NOs: 15, 16 and 17) provided frequencies of 62.5% for tgc for the group. The disclosed disparity of 100% to 62.5% from applying the codon-optimised nucleotide sequence of SEQ ID NO: 63 as an *exemplification* of the invention (examples, with respect to *E. coli*) thus supported that feature (ix) was not limiting on feature (x) in claim 1 as granted.

22.3 Granted claim 1 also allowed for a deviation between the codon frequency in the group according to feature (ix) and the codon frequency in the nucleic acid sequence according to feature (x) due to the sequential nature of the procedure defined in granted dependent claims 5 and 7 (now features (xi) and (xii) in claim 1 of the main request, see sectionII.) providing the rules for placing the codons of the motifs in the nucleic acid sequence to be expressed, i.e. in a step-by-step manner starting from the first codon of the corresponding motif at the N-terminus. These rules thus demonstrated that the number of amino acid residues in the polypeptide could deviate from the number of codons in the motif or a multiple of this number. More residues of the amino acid being present in the polypeptide than codons occurring in the motif meant having to start again with the first codon of the

motif (see granted claim 7). Granted claim 1 thus *expressly* envisaged the deviation, and feature (ix) thus needed "to cover" such a deviation.

22.4 Finally, although the patent did not provide a definition of the term "about the same" in features (viii) and (ix) of granted claim 1, Article 69(1) EPC provided that for the scope of such a claim, the description and the drawings may be consulted. Thus, having regard to the disclosure in the patent, including the examples, the term "about the same" in feature (ix) was understood as meaning "at least" or "the same and more" to account for the application of the claimed method according to the invention to polypeptides, where a complete motif cannot be used due to a smaller number of occurrences of the specific amino acid residue than in the motif.

22.5 The appellant concluded that, given the disclosure of the patent as a whole and the skilled person's synthetical propensity to arrive at a technically sensible interpretation of a claim (see decision T 190/99, Catchword), the mandatory application of the motifs to each expressed polypeptide, including where codon frequencies did not match between group and polypeptide, was covered by granted claim 1. Legal certainty thus required that limiting the claim to this embodiment could not cause an extension of the protection provided by claim 1 of the main request.

23. In consideration of the appellant's first line of argument, the board came to the conclusion that the scope of protection of claim 1 as granted is in accordance with the provisions in features (iv) to (viii), (ix) and (x) (see section I.), each having a different wording and technical meaning and providing

different limitations to the codon usage for designing the coding sequence (see point 16. above) and, furthermore, that the restrictions of feature (ix) in claim 1 as granted have a limiting effect on the codon usage of those amino acids referred to in granted claim 1 which are chosen to be optimised in the claimed method (see point 20. above).

24. The board agrees with the appellant that when considering a claim, the skilled person should rule out interpretations which are illogical or which do not make technical sense, i.e. should try, with synthetical propensity, i.e. building up rather than tearing down, to arrive at an interpretation of the claim which is technically sensible and takes into account the whole disclosure of the patent (Article 69 EPC). A patent must be construed by a mind willing to understand, not a mind desirous of misunderstanding (see CLBA, II.E.2.3.3).

25. However, the board cannot agree with the appellant that the results of the opposition division's exemplary calculations are artificial or extreme to the extent that they do not correspond to a "real world" situation of a polypeptide intended to be expressed and recovered in accordance with claim 1 as granted and of the main request, respectively. Indeed, when giving the features of claim 1 of the main request the meaning as understood by the skilled person, neither the calculations nor their results can be held to be nonsensical.

26. The deviation in the codon frequency between the group and the polypeptide-encoding nucleic acid in the example relied on by the appellant (see point 22.2 above), i.e. 100% versus 62.5%, supports the real-world

nature of the opposition division's calculations. The board moreover agrees with the respondent that the expression and recovery of the polypeptide encoded by SEQ ID NO: 63 is not covered by claim 1 as granted, i.e. is not an exemplification of the claimed invention, contrary to the appellant's submission.

27. The board agrees with the opposition division and sees, even having regard to granted dependent claims 5 and 7 (see point 22.3), no room to conclude that feature (ix) in claim 1 of the patent as granted provided that a codon usage frequency of 80% (in the case of the gcc codon for expressing a polypeptide comprising five Ala residues) was "about the same" as the codon usage frequency of 40% within the group used as the reference in feature (ix) in granted claim 1. In the opinion of the board, such an interpretation lacked any technical sense and deprived feature (ix) in granted claim 1 of its technical meaning.

28. The board also finds illogical and not to make technical sense the appellant's submission that given the disclosure in the patent, including the examples, the term "about the same" in feature (ix) had to be understood as meaning "at least" or "the same and more" to account for the application of the claimed method according to the invention to polypeptides, where a complete motif cannot be used due to there being a smaller number of occurrences of the specific amino acid residue than in the motif (see point22.4), i.e. to not limit the method of claim 1 as granted to only express and recover polypeptides where the number of residues of the amino acids with codon degeneracy corresponds to the number of codons in the respective motifs or a multiple of that number. Finally, the board agrees with the respondent that the appellant's

submissions on the term "about the same" amount to extending its meaning to encompass something that is "not the same at all", contrary to the ordinary meaning of the term "about the same" in the English language.

Conclusion

29. In view of the above considerations, the deletion of the feature "wherein the usage frequency of a codon in the polypeptide encoding nucleic acid is about the same as its specific usage frequency within its group" in claim 1 of the main request extends the scope of protection compared to granted claim 1 and, therefore, infringes Article 123(3) EPC. Thus, the appeal is unallowable.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chair:

L. Malécot-Grob R. Morawetz

Decision electronically authenticated