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Datasheet for the decision of 6 May 2021

Case Number: T 1251/16 - 3.3.01

Application Number: 07752636.6

Publication Number: 1996220

IPC: A61K38/16, C12N15/10

Language of the proceedings: EN

Title of invention:
UNSTRUCTURED RECOMBINANT POLYMERS AND USES THEREOF

Patent Proprietor:
Amunix Operating Inc.

Opponents:
Novo Nordisk A/S
XL-protein GmbH

Headword:
Unstructured recombinant polymers/AMUNIX

Relevant legal provisions:
EPC Art. 123(2), 83, 111(1)
RPBA Art. 12(4), 13(1), 15(3)
EPC R. 115(2)

Keyword:

Amendments - intermediate generalisation
Sufficiency of disclosure - (yes)
Appeal decision - remittal to the department of first instance (yes)

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Case Number: T 1251/16 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 6 May 2021

Appellant: (Patent Proprietor)	Amunix Operating Inc. 500 Ellis Street Suite B Mountain View, CA 94043 (US)
Representative:	Mewburn Ellis LLP City Tower 40 Basinghall Street London EC2V 5DE (GB)
Respondent: (Opponent 1)	Novo Nordisk A/S Novo Allé DK-2880 Bagsvaerd (DK)
Representative:	D Young & Co LLP 120 Holborn London EC1N 2DY (GB)
Respondent: (Opponent 2)	XL-protein GmbH opposition withdrawn
Representative:	

Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 16 March 2016 revoking European patent No. 1996220 pursuant to Article 101(3)(b) EPC**

Composition of the Board:

Chairman	A. Lindner
Members:	T. Sommerfeld
	R. Romandini

Summary of Facts and Submissions

I. European patent 1996220 is based on application 07752636.6, which was filed as an international application and published as WO 2007/103515. The patent is entitled "Unstructured recombinant polymers and uses thereof" and was granted with 11 claims.

Claim 1 as granted read as follows:

"1. A method of increasing the serum half-life of a protein, comprising:

fusing said protein with one or more unstructured recombinant polymers (URPs), wherein the URP comprises at least about 200 contiguous amino acids, and wherein

(a) the sum of glycine (G), aspartate (D), alanine (A), serine (S), threonine (T), glutamate (E) and proline (P) residues contained in the URP, constitutes more than about 80% of the total amino acids of the URP; and
(b) at least 50% of the amino acids of the URP are not present in secondary structure as determined by Chou-Fasman algorithm; and wherein said URP is substantially incapable of non-specific binding to a serum protein; and
(c) the URP has a Tepitope score equal to or less than -4."

II. Two oppositions were filed against the granted patent, both opponents requesting revocation of the patent in its entirety on the grounds of lack of novelty and inventive step (Articles 54(2) and 56 EPC and Article 100(a) EPC), lack of sufficiency of disclosure (Article

100(b) EPC) and added subject-matter (Article 100(c) EPC).

III. With a letter dated 30 September 2015, opponent 2 withdrew its opposition.

IV. By its decision pronounced at oral proceedings, the opposition division revoked the patent under Article 101(2) and 101(3)(b) EPC.

The opposition division decided that the claim sets according to the main request (claims as granted), in particular claim 9, contravened Article 123(2) EPC and that the claim sets according to the auxiliary requests (first to seventh) contravened Article 83 EPC. Moreover, the opposition division decided that documents D43, D45 to D51, D53 and D54 were not to be admitted into the proceedings.

V. The patent proprietor (appellant) lodged an appeal against that decision. With the statement of the grounds of appeal, dated 22 July 2016, the appellant requested that the patent be maintained as granted (main request) or, alternatively, according to the first to seventh auxiliary requests, all re-filed with the grounds of appeal. New documents D62 and D63 were submitted.

The **main request** consists of the claims as granted.

The **first auxiliary request** differs from the main request in that claim 9 has been deleted.

VI. In its letter of reply, the opponent (respondent) requested that the appeal be dismissed. It also requested that documents D46 to D51 be admitted into

the proceedings and submitted new documents, D64 to D76.

VII. The appellant replied by letter dated 8 September 2017, requesting that the decision of the opposition division not to admit documents D46 to D51 be confirmed and that new documents D64, D65 and D67 to D76 not be admitted. It also submitted document D77 as a reaction to documents D73 and D74.

VIII. The respondent submitted a further letter, accompanied by new document D78.

IX. Summons for oral proceedings before the board were issued, followed by a communication pursuant to Article 15(1) RPBA, providing the board's preliminary opinion on some issues.

X. By letters dated 23 March 2021 and 16 April 2021, the respondent informed that it would not attend oral proceedings.

XI. Oral proceedings before the board took place on 6 May 2021, by videoconference as requested by the only participating party. At the end of oral proceedings, the chairman announced the decision.

XII. The documents cited during the proceedings before the opposition division and the board of appeal include the following:

D2 Chou PY & Fasman GD, Biochemistry 1974, 13: 222-245

D18 Sturniolo T et al., Nature Biotechnol. 1999, 17: 555-561

D32 Alters SE et al., PLoS One 2012, 7(11): e50630

D33 Yuen KCJ et al., J Clin Endocrinol Metab. 2013, 98: 2595-2603
D42 Tepitope implementation output for (GPP)67 peptide from motif of D4
D55 CF scores for 50 sequences listed in the right-hand side column of D31
D56 Comparison of the CF scores of D31 with the CF scores derived from D55
D58 Tepitope analysis of the sequence of Fig. 1, D14
D60 Tepitope analysis of the sequence of Fig. 3, D14
D61 CF scores for left-hand side column of D31
D63 Tepitope values for random 200mer sequences composed of the amino acids GADSTEP
D65 Atkins and de Paula, Atkins' Physical Chemistry (8th Ed; 2006) WH Freeman and Company (NY, USA)
D66 USPTO Final Office Action for US 11/715,296

XIII. The appellant's submissions, in so far as relevant for the present decision, may be summarised as follows.

Main request, Article 100(c) EPC

The passage in paragraph [0121] of the application as filed represented a general statement. The application put an enormous emphasis on unstructured recombinant polymers (URPs) comprising amino acids of the so-called GADSTEP group, as was evident from originally filed claims 1, 2, 11, 12, 16, 37, 38 and 55, as well as paragraph [0108]. Granted claim 9 did not offer anything new over the teaching of the application as filed because its subject-matter was disclosed in paragraph [0121] in combination with the rest of the application. Reference to paragraph [0113] was not even needed, but in any case there was no incompatibility between paragraphs [0113] and [0121]. The subject-matter of claim 9 could not be considered an

intermediate generalisation. While the application did disclose several embodiments, it was undisputed that the embodiment with the GADSTEP amino acids was the most prominent of them.

Auxiliary request 1, Article 83 EPC

The opposition division erred in its conclusions and in particular conflated the separate requirements of Articles 84 and 83 EPC. In the case at issue, carrying out the invention meant being able to provide the URPs which solved the technical problem, and there was ample teaching in the specification to explain and provide the URPs. Not only did the specification describe the technical basis for the half-life extension by the claimed URPs, but it also included data on some of the properties of the URPs and fusions comprising them. The patentee had provided evidence that the URPs could be prepared according to this teaching and that these URPs would have the properties ascribed to them (D32, D33). There was no evidence on file that the person skilled in the art would have been unable to carry out the invention based on the patent specification.

The skilled person would have had no difficulty in performing the tests for the Chou-Fasman (CF) and the Tepitope scores. The opposed patent taught to use the CF algorithm to determine secondary structure. As computer programs implementing the CF algorithm were available and generally accepted for determining secondary structure, the person skilled in the art would not have needed more information than the reference to the algorithm to find an appropriate computer program and to use it. Contrary to the conclusions of the opposition division, it was clear

that the definition of (absence of) secondary structure given in the claim was that according to CF in D2.

Similarly, the Tepitope algorithm was referred to throughout the specification, its purpose being to confirm an absence of likely T cell epitopes (paragraph [0122], explicitly cross-referencing D18). To use a Tepitope server all that would be required was the pasting-in of an amino acid sequence; any other user variables were clearly taught in D18. The output of the algorithm was a set of scores for each 9mer in the protein, and the skilled person could then have assessed the feature of the claim by merely confirming that no score was -4 or higher. Following this process, consistent scores would reliably be obtained for the same sequence, as was evidenced by D63.

As to the feature of serum binding, the patent described a test for determining whether a URP is "capable" of binding serum proteins (e.g. paragraph [00337]). Finally, in respect of the "half-life" feature, the feature was a purposive and relative one that did not even require quantitation. Hence, it was irrelevant that there might be different methods for measuring half-life leading to different results.

In summary, there would have been no undue burden to produce URP fusions having the structural features of the claims; the functional properties of the URPs in the fusions could have been readily assessed in the light of the specification; and the technical effect ascribed to the URP fusions could have been readily achieved and verified. It was also important to note that the structural features and functional properties of the URPs were related.

XIV. The respondent's arguments, in so far as relevant for the present decision, may be summarised as follows.

Main request, Article 100(c) EPC

The combination of paragraphs [0113] and [0121] would not have been envisaged by the person skilled in the art because paragraph [0121] was silent on what group of amino acids, if any, the repeated amino acids should be selected from. Moreover, the disclosure as a whole was hugely inconsistent on the amino acids which should be "preferred" or "enriched" in the URPs (e.g. paragraphs [0108], [0120], [0122] and [0129], which each referred to different groups of amino acids). Thus, it was not apparent that amino acids other than GADSTEP should be excluded.

Auxiliary request 1, Article 83 EPC

To carry out the invention, preparing a URP according to the definition in the claims was essential. However, this was not enabled by the disclosure of the specification. In view of ill-defined parameters, the skilled person would not have been able to unequivocally identify whether something was a URP according to the invention. Such ill-defined parameters would thus necessarily lead to situations where it was arbitrary whether a particular embodiment fell within the scope of the claims, with no guidance from the patent whatsoever; embodiments incapable of solving the technical problem would fall within the scope of the claims. Several arguments made by the appellant concerned reading limitations which did not exist in the wording of the claims. However, the claim was to be read based on the ordinary wording of the claim and not

on the basis of something appearing in the description only.

The CF algorithm did not output a straightforward value of "% amino acids in secondary structure". According to common general knowledge as represented by D65, the definition of secondary structure meant that all amino acids in a protein have a secondary structure since they all contribute to the protein backbone chain and thus the spatial arrangement. Thus, the percentage of amino acids not in a secondary structure according to the CF algorithm would always be 0. Contrary to the conclusions of the opposition division, coils were not necessarily non-structured parts of a protein (D65, page 668). The claim simply defined a URP as having at least 50% of amino acids not in secondary structure - whether this secondary structure was highly ordered (e.g. in the form of helices or sheets) was irrelevant. The claim did not refer to D2 or the CF algorithm as a definition for secondary structure, and D2 did not define secondary structure either. Rather, D2 defined an algorithm able to predict specific elements of secondary structure within proteins, and these did not exclude coils. Likewise, the two references to secondary structure in the patent (in paragraphs [0077] and [0100]) also referred to "unstructured loops" and "random coil structures", respectively. Whether beta turns were included in the score calculation was important because the score would change drastically accordingly, as shown in D55, D56 and D61.

As to the Tepitope scores, there were also major inconsistencies regarding how they were calculated, as shown using the tool referenced by D18 (the only reference given in the patent) in, for example, D42, D58 and D60. The data provided by the appellant had a

number of shortcomings. For instance, in D63, it was not clear what specific tool was used, reference being only made to "the Tepitope software". Moreover, there was no evidence for using the software for calculating a Tepitope score for an entire peptide. Rather, the algorithm was used to find likely binding peptides from larger sequences using a defined threshold such as 5%, as was shown in peer-review articles. Table 2 of D18 only listed the available HLA-DR matrices in Tepitope (at the time of publication). As correctly judged by the opposition division, there was a significant gap in the disclosure of the patent as to how a single Tepitope score could be derived for a peptide of at least 200 amino acids since Tepitope scores could only be given for 9mers within that peptide. Several arithmetic derivations were possible (e.g. summation, mean and median), the choice of which was not taught in the patent but would necessarily lead to several distinct "Tepitope scores" being derivable for any given URP.

The feature that the URPs should not have unspecific serum binding could be interpreted as just requiring that they did not bind to one serum protein but that they could bind to all others. Moreover, there was no instruction on what proteins should be tested.

As to the feature "serum half-life", substantially different methods to assess serum half-life were referred to in the patent, and no instruction was given on which to use. It was, however, highly unlikely that the same results would be obtained when using different tests (e.g. in vivo and in vitro).

XV. The appellant requests that the appealed decision be set aside and that the patent be maintained as granted

(main request) or, alternatively, according to the first to seventh auxiliary requests, all filed with the grounds of appeal. It moreover requests that the decision of the opposition division not to admit documents D46 to D51 be confirmed and that new documents D64, D65 and D67 to D76 not be admitted. It also requests that documents D62 and D63, filed with the statement of grounds of appeal, be admitted, and that document D77, filed with the letter of 8 September 2017, be admitted if documents D73 and D74 are admitted.

The respondent requested in writing that the appeal be dismissed. It also requested that documents D46 to D51, D64 to D76 and D78 be admitted into the proceedings.

Reasons for the Decision

1. The appeal is admissible.

2. As announced by letters dated 23 March 2021 and 16 April 2021, the respondent was not represented at oral proceedings. In accordance with Rule 115(2) EPC, if a party duly summoned to oral proceedings does not appear as summoned, the proceedings may continue without that party. As stipulated by Article 15(3) RPBA, the board is not obliged to delay any step in the proceedings, including its decision, by reason only of the absence at the oral proceedings of any party duly summoned that may then be treated as relying on its written case.

3. Main request, Article 100(c)/123(2) EPC

3.1 In accordance with Article 123(2) EPC, the European patent application or the European patent must not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed. The "gold standard" for assessing compliance with Article 123(2) EPC is that any amendment to the parts of a European patent application or European patent relating to the disclosure may only be made within the limits of what the skilled person would have derived directly and unambiguously, using the common general knowledge available at the date of filing, from the whole of these documents as filed.

3.2 Claim 9 as granted reads as follows:

"9. The method of claim 1, wherein said URP contains only 3, 4, 5, or 6 different types of amino acids selected from the group consisting of glycine (G), aspartate (D), alanine (A), serine (S), threonine (T), glutamate (E) and proline (P)."

3.3 The board agrees with the conclusions of the opposition division that claim 9 of the main request adds subject-matter contrary to the requirements of Article 123(2) EPC. In particular, there is no basis for the feature "wherein the URP contains only 3, 4, 5, or 6 different amino acids selected from the group consisting of ... [GADSTEP]".

3.4 The appellant indicated paragraph [0121] "in combination with the rest of the application" or possibly paragraph [0113] of the application as filed as constituting a basis for this feature. The relevant passage in paragraph [0121] reads "URPs or the repeats

inside URPs often contain only 1, 2, 3, 4, 5 or 6 different types of amino acids". It does not refer to any group of amino acids from which to select the different types of amino acids, and it is therefore interpreted as referring to any possible amino acid. Paragraph [0113], on the other hand, discloses that "Where desired, URPs can be designed to contain (...) sometimes only a few types of amino acid, e.g., two to five types of amino acids (e.g., selected from G, E, D, S, T, A and P)". This passage, while referring to the GADSTEP group, only envisages the use of two to five, rather than three to six (as in the claim), types of amino acids from this group. Hence, the two passages do not provide an adequate basis for the disputed feature.

3.5 While the board agrees with the appellant's argument that literal support is not necessarily required for the purposes of Article 123(2) EPC, this does not mean that different passages of the originally filed documents can be freely combined to come up with a teaching that is not unambiguously derivable from the application as filed.

3.6 The appellant further argued that the application was focused on the use of URPs comprising amino acids of the GADSTEP group and that therefore the skilled person would have read any general statements such as the one in paragraph [0121] within this context. The board agrees that URPs comprising GADSTEP amino acids are frequently mentioned in the application but so are other types of URPs, such as glycine-rich URPs (e.g. paragraph [0111] and following), URPs containing non-glycine residues (paragraph [0118] and following) and URPs derived from human sequences (paragraph [0122] and following). Accordingly, the disclosure of paragraph [0121] referring to URPs comprising only one to six

different types of amino acids would not have been implicitly interpreted as meaning one to six different amino acids of the GADSTEP group.

3.7 The board thus comes to the conclusion that claim 9 of the main request adds subject-matter contrary to Article 123(2) EPC. The main request is thus not allowable.

3.8 On page 5 of the letter of reply to the grounds of appeal, the respondent stated that it maintained its objections for added subject-matter also in relation to claims of the main request other than claim 9. These objections were decided upon in the appealed decision, the opposition division having come to the conclusion that they were not valid. Hence, if the respondent still wanted to rely on these objections in appeal, it should have submitted its arguments why the opposition division was wrong in this respect. In the absence of any such arguments, the board sees no reason to deviate from the conclusions of the opposition division. Hence, the board considers that the other claims of the main request fulfil the requirements of Article 123(2) EPC.

4. Auxiliary request 1, Article 83 EPC

4.1 Claim 1 of auxiliary request 1 is directed to a method of increasing the serum half-life of a protein, comprising fusing this protein with one or more URPs, the URP being further defined by a number of structural and functional features as follows (for the exact wording of the claim, see section I): it comprises at least about 200 contiguous amino acids; the sum of glycine (G), aspartate (D), alanine (A), serine (S), threonine (T), glutamate (E) and proline (P) residues contained in the URP constitutes more than about 80% of

the total amino acids of the URP; at least 50% of the amino acids of the URP are not present in secondary structure as determined by the CF algorithm; it is substantially incapable of non-specific binding to a serum protein; and it has a Tepitope score equal to or less than -4.

4.2 Being a method claim, the purpose of the method, which is increasing the serum half-life of a protein, is a limiting feature of the claim. Hence, only embodiments that achieve this effect are part of the claim. For the purposes of sufficiency of disclosure, the application must thus provide an enabling disclosure of the URPs as claimed and must also show or at least render it plausible that use of these URPs in a method as claimed achieves the effect of increasing the serum half-life of a protein.

4.3 In the board's view, the patent fulfils both conditions. It discloses how to produce URPs with the features as claimed, and it also describes the technical basis for the half-life extension of a protein when using a URP as claimed, thus rendering it plausible that such a URP can be successfully used in a method for increasing serum protein half-life as claimed. Post-published data in documents D32 and D33 confirm that this effect is achieved for two fusion proteins comprising pharmaceutical proteins and a URP according to the invention.

4.4 The respondent argued that preparing a URP according to the definition in the claims was not enabled by the disclosure in the patent because the skilled person would not have been able to unequivocally identify whether something was a URP according to the invention. In view of parameters which were ill-defined, it would

be essentially arbitrary whether a particular embodiment would fall within or outside the scope of the claims. In particular, the features of items (b) and (c), namely "at least 50% of the amino acids of the URP are not present in secondary structure as determined by Chou-Fasman algorithm", "URP is substantially incapable of non-specific binding to a serum protein" and "URP has a Tepitope score equal to or less than -4", were considered to be such ill-defined parameters.

4.5 First, the board notes that any URPs that do not achieve the technical effect will not be encompassed by the claim, as explained above. Moreover, the respondent has not provided any evidence of any such embodiment. Second, the URPs as claimed are already structurally defined as having at least 200 amino acids, of which more than 80% should be of the GADSTEP group. Accordingly, the skilled person would have already known that, for a URP of 200 amino acids, at least 160 of them should be selected from G, A, D, S, T, E or P and would only have had to decide on the remaining 40 or less amino acids and on the order of the amino acids in the sequence. As further explained below, the board considers that, with the teaching of the patent, the skilled person could have made the necessary decisions to produce the URPs according to the invention without undue burden.

4.6 The skilled person would have known from the patent application (e.g. paragraph [0075]) that the term "unstructured recombinant polymer" (URP) refers to amino acid sequences that share commonality with denatured peptide sequences, i.e. peptide sequences in "denatured conformation" or "unfolded conformation". This is defined in the preceding paragraph as referring

to a state of a peptide in solution that is characterised by a large conformational freedom of the peptide backbone. Paragraph [0075] further teaches that URP sequences lack a defined tertiary structure and have limited or no secondary structure as detected by, e.g. the CF algorithm. Paragraph [0102], which again defines the URPs as comprising "amino acid sequences that typically share commonality with denatured peptide sequences under physiological conditions", goes on to teach that "A variety of methods have been established in the art to ascertain the second and tertiary structures of a given polypeptide", these methods including CD spectroscopy and "computer programs or algorithms such as the Chou-Fasman algorithm (Chou, P. Y., et al. (1974) Biochemistry, 13: 222-45)", the cited reference being document D2 in the proceedings. The algorithm is able to predict, for a given URP sequence, "whether there exists some or no secondary structure at all".

4.7 The following paragraph (paragraph [0103]) then teaches that "The subject URPs can be sequences with low immunogenicity" and that "Low immunogenicity can be a direct result of the conformational flexibility of URP sequences", preferred URPs being "designed to avoid formation of conformational epitopes". Possible sequences with low immunogenicity can be "sequences having a low tendency to adapt compactly folded conformations in aqueous solution" and "low immunogenicity can be achieved by choosing sequences that resist antigen processing in antigen presenting cells, choosing sequences that do not bind MHC well and/or by choosing sequences that are derived from human sequences". Paragraph [0125] further teaches how to design URP sequences that are "substantially free of epitopes recognized by human T cells" by synthesising

"a series of semi-random sequences with amino acid compositions that favor denatured, unstructured conformations and evaluate these sequences for the presence of human T cell epitopes and whether they are human sequences" by using known assays. One possible approach is "to design URP sequences that result in low scores using epitope prediction algorithms like TEPITOPE (Stumiolo, T., et al. (1999) *Nat Biotechnol*, 17: 555- 61 [document D18 in the proceedings])".

4.8 Paragraph [0100] further teaches that the URP should be designed to minimise interaction with (i.e. binding to) serum proteins, including antibodies. It states that "Different URP designs can be screened for serum protein binding by ELISA, immobilizing the serum proteins and then adding the URP, incubating, washing and then detecting the amount of bound URP". Two approaches are further disclosed, and the patent then states that "Using these approaches we have designed our URPs to show very low levels of binding to serum proteins".

4.9 Paragraph [0108] provides specific teaching concerning the preferred amino acids to be used in the construction of URPs. It refers to the predominance of hydrophilic amino acids such as glycine, serine, aspartate, glutamate, lysine, arginine and threonine (GADSTEP) and teaches that tryptophan, phenylalanine, tyrosine, leucine, isoleucine, valine and methionine are "Hydrophobic residues that are less favored in construction of URPs". It also teaches in paragraph [0109] that "As a result of their amino acid composition, URP sequences have a low tendency to form aggregates in aqueous formulations and the fusion of URP sequences to other proteins or peptides tends to enhance their solubility and reduce their tendency to

form aggregates, which is a separate mechanism to reduce immunogenicity". Paragraph [0110] then teaches that "URP sequences can be designed to avoid certain amino acids that confer undesirable properties to the protein. For instance, one can design URP sequences to contain few or none of the following amino acids: cysteine (to avoid disulfide formation and oxidation), methionine (to avoid oxidation), asparagine and glutamine (to avoid desamidation)".

4.10 Hence, the patent application provides detailed teaching on how to obtain URPs suitable for use in the method as claimed. It also makes clear that the functional properties of the claimed URPs derive from their structural features. Hence, while these functional features may not be very clearly defined in the claims, this would not have hindered the skilled person from carrying out the invention without undue burden.

4.11 The board agrees with the respondent that the feature "at least 50% of the amino acids of the URP are not present in secondary structure as determined by Chou-Fasman (CF) algorithm" is unclear. In fact, it is common general knowledge, evidenced by, for example, D65, that all amino acids in a protein are part of a secondary structure since they all contribute to the protein backbone chain and thus to the spatial arrangement, independent of them being part of a highly ordered secondary structure, such as helices or sheets, or of non-ordered secondary structures such as random coils or unstructured loops. This definition is also in agreement with the patent's disclosure in paragraphs [0077] and [0100], referring to "unstructured loops" and "random coil structures", respectively. The implementation of the CF algorithm, described in D2,

also does not exclude coils as secondary structure, as extensively argued by the respondent. According to this definition of secondary structure, all amino acids of a URP will be found to be present in "secondary structure" and the percentage of amino acids not in secondary structure according to the CF algorithm would always be 0. It is also true, as argued by the respondent on basis of documents D55, D56 and D61, that the CF scores can change drastically depending on whether some secondary structure types (e.g. beta turns) are taken into account.

4.12 While the above is true, the board considers that the skilled person would still have been in a position to decide what URPs were according to the claim. It follows from the definition itself of URPs (given in the patent, for instance, in paragraphs [0075] and [0102], see above) that these should have a "denatured conformation" or "unfolded conformation" and that this is what is meant by having little or no secondary structure. It would therefore have been immediately obvious to the skilled person reading the patent application that the URPs according to the invention should have few to no highly ordered structures such as helices and sheets and rather have more unordered structures such as random coil. The skilled person would thus have known how to apply the CF algorithm accordingly, i.e. which secondary structures should be taken into account to end up with a URP with "unstructured conformation".

4.13 The respondent also argued that it was not clear how the Tepitope score was to be calculated and that there were major inconsistencies as shown for instance in D42, D58 and D60. Moreover, it was not apparent how the score should be evaluated for a whole peptide of 200

amino acids since the algorithm was in fact designed for 9mers within a peptide. The board agrees that there might be a lack of clarity as to how the Tepitope score is to be calculated but again considers that the disclosure of the patent application would have put the skilled person in a position to be able to determine which URPs were part of the invention. As mentioned above, the patent application teaches (paragraph [0125]) how to design URP sequences that are "substantially free of epitopes recognized by human T cells" and that these sequences can be evaluated for the presence of human T cell epitopes by using known assays such as the Tepitope disclosed in D18. It would also have been clear for the skilled person that, when calculating the Tepitope score for larger peptides, it would be important that none of the 9mers within the peptide had a score over -4; anything else would not make sense in the context of the patent. The post-published document D63 moreover confirms that URPs meeting the Tepitope criteria of the claims could be readily provided by following the teaching of the specification. For these purposes, it is irrelevant that it is not clear what specific "Tepitope software" tool was used in D63 because the claim is also not limited to any specific tool being used.

4.14 Finally, while the feature "substantially incapable of non-specific binding to a serum protein" may be unclear, the patent application again teaches what is meant by such a feature and how to test it (paragraph [0100], see above). Similarly, the respondent's objection concerning the "serum half-life" feature is also not convincing. It is true that different methods of assessing serum half-life can be used which may lead to different results. However, since the claim requires only that there is an increase in serum half-life, it

is not relevant what the absolute values are and whether they differ according to the method used.

4.15 The board thus comes to the conclusion that claim 1 of the auxiliary request fulfils the requirements of Article 83 EPC.

5. Admission of documents

Documents D46 to D51, D53 and D54

5.1 All these documents were submitted during the proceedings before the opposition division, and the opposition division decided not to admit them into the proceedings. In the appeal proceedings, the respondent requested that documents D46 to D51 be admitted into the proceedings, while the appellant requested that the decision of the opposition division not to admit documents D46 to D51 be confirmed. The appellant also appears to have contested the decision of the opposition division not to admit D53 and D54.

5.2 In the communication pursuant to Article 15(1) RPBA, the board gave its preliminary opinion that it did not see any reason to deviate from the decision of the opposition division not to admit documents D46 to D51 into the proceedings. It noted that the appellant had not relied on D53 or D54 in its submissions and that there was therefore no apparent reason to rule on the admission of these documents.

5.3 The parties have not provided any further arguments concerning the admission of these documents. Hence, the board sees no reason to overrule the decision of the opposition division not to admit these documents into

the proceedings. Documents D46 to D51, D53 and D54 are therefore not admitted into the proceedings.

Documents D62 to D78

5.4 Documents D62 to D78 have all been submitted during appeal proceedings: D62 and D63 by the appellant with the statement of grounds of appeal; D64 to D76 by the respondent with the reply to the grounds of appeal; and D77 and D78 by the appellant and the respondent, respectively, in further letters. The appellant requested that new documents D64, D65 and D67 to D76 not be admitted.

5.5 In the communication pursuant to Article 15(1) RPBA, the board gave its preliminary opinion that it was inclined to admit documents D62 and D63 into the proceedings and that it was not apparent why documents D64 to D76 should be admitted into the proceedings.

5.6 There have been no further arguments from the parties concerning the admission of these documents. Since documents D62 and D63 were filed with the statement of grounds of appeal and the respondent did not object to their admission, the board decided to use its discretion pursuant to Article 12(4) RPBA to admit them into the proceedings. As to the further documents, the following is noted.

5.6.1 D65 is an extract of a physical chemistry textbook providing a definition of secondary structure. The board sees no reason not to admit a document which is simply evidence of the common general knowledge at the relevant date. Hence, document D65 was admitted into the proceedings.

5.6.2 The appellant had no objections against the admission of document D66, which consisted of an official communication of the USPTO concerning the proceedings to which declaration D30 related. The board therefore also decided to admit this document into the proceedings.

5.6.3 The remaining documents have not been considered relevant for the present decision. They consisted of the well-known UKHL Kirin-Amgen vs. Hoechst Marion Roussel decision (D64); CF scores for different proteins (D67 to D69) and for randomly generated "URPs" (D70) as well as a summary of D70 results (D71); a second declaration of Professor Sternberg (D72); Tepitope for the first set of sequences from D30, exhibit 2 (D73) and for the first 200mer GADSTEP sequence of D63 (D74); two prior art scientific publications where Tepitope has been used (D75 and D76); an answer to an enquiry to the providers of the IEDB Tepitope server (D77); and a letter from the patentee submitted during the examination proceedings of the case at issue (D78). The board found it appropriate not to decide on the admission of these documents in view of the decision to remit the case for further prosecution (see below).

6. Remittal for further prosecution

6.1 Under Article 111(1) EPC, the boards, following examination on the allowability of the appeal, must decide on the appeal and may either exercise any power within the competence of the department which was responsible for the appealed decision or remit the case to that department for further prosecution. The boards may remit a case for further prosecution if essential questions regarding the patentability of the claimed

subject-matter have not yet been examined by the department responsible for the appealed decision and their handling in appeal would imply a significant burden.

6.2 In the present case, the opposition division reached a decision on Article 123(2) and 83 EPC but did not discuss, let alone decide on, any other of the remaining opponents' objections, namely under Articles 54 and 56 EPC. Both parties were of the opinion that the case should be remitted to the department of first instance for discussion of these issues. The board considers that an exhaustive analysis of these aspects would imply a burden which makes it appropriate to remit the case to the department of first instance for further prosecution.

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:

M. Schalow A. Lindner

Decision electronically authenticated