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Case Number: T 0308/20 - 3.3.04

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Language of the proceedings: EN

Title of invention:
Immunomodulatory therapy for type 1 diabetes mellitus autoimmunity

Applicants:
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Jalahej, Heyam
Daubeney, Nara
Daubeney, Piers

Headword:
Preproinsulin fragments vaccine/TIHAMER

Relevant legal provisions:
EPC Art. 84, 111(1), 123(2)
RPBA 2020 Art. 13(2)

Keyword:

Amendments - main request, auxiliary requests 1 and 6, added subject-matter (yes)
Claims - and/or connectors - auxiliary requests 2 to 5, clarity (no) - auxiliary request 8 -clarity (yes) - amendments - auxiliary request 8 - allowable (yes)
Amendment after summons - auxiliary request 7 - exceptional circumstances (no)
Appeal decision - remittal to the department of first instance (yes)

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Case Number: T 0308/20 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 9 June 2022

Appellant: (Applicant 1)	Orban, Tihamer Flat 17 Lyle Park 57 Putney Hill London SW15 6RT (GB)
Appellant: (Applicant 2)	Jalahej, Heyam Flat 17 Lyle park 57 Putney Hill London SW15 6RT (GB)
Appellant: (Applicant 3)	Daubeney, Nara 9 Hazlewell Road Putney, London SW15 6LU (GB)
Appellant: (Applicant 4)	Daubeney, Piers 9 Hazlewell Road Putney, London SW15 6LU (GB)
Representative:	Forresters IP LLP Skygarden Erika-Mann-Straße 11 80636 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 6 September 2019 refusing European patent application No. 15708257.9 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairwoman	M. Pregetter
Members:	O. Lechner
	L. Bühler

Summary of Facts and Submissions

I. The applicants ("appellants") filed an appeal against the examining division's decision to refuse the European patent application No. 15 708 257.9 ("application"), entitled "*Immunomodulatory therapy for type 1 diabetes mellitus autoimmunity*".

II. The examining division decided, *inter alia*, the following:

- The set of claims of the main request and auxiliary requests 1, 4 and 5 contained subject-matter which extended beyond the content of the application as filed (Article 123(2) EPC);
- claim 1 of auxiliary requests 2 and 3 were unclear (Article 84 EPC); and
- claim 1 of auxiliary requests 2 to 5 did not involve an inventive step (Article 56 EPC).

III. With their statement of grounds of appeal, the appellants filed a new main request and new auxiliary requests 1 to 6.

IV. The board summoned the appellants to oral proceedings. In a communication under Article 15(1) RPBA, the board provided a preliminary assessment of the appeal. The board held, *inter alia*, the following:

- Claim 1 of the main request and auxiliary requests 1 and 6 was not clearly and unambiguously derivable from the content of the application as filed (Article 123(2) EPC);
- claims 1 and 7 of auxiliary requests 2 and 4 as well as claims 1 and 4 of auxiliary request 3 and 5 were ambiguous (Article 84 EPC); and

- the use of multiple "and/or" connectors in several claims of the main request and the auxiliary requests could possibly lead to a lack of clarity (Article 84 EPC).

V. By letter dated 17 May 2022, the appellants submitted arguments addressing issues raised in the board's preliminary opinion. They also submitted new auxiliary requests 7 to 12 together with a declaration by Mr Tihamer Orban.

VI. By letter dated 25 May 2022, the appellants submitted new auxiliary requests 13 and 14.

VII. During the oral proceedings, the appellants filed a new auxiliary request 7 replacing auxiliary request 7 (submitted on 17 May 2022).

Claims 1 and 7 of the application as filed read:

"1. A composition comprising a therapeutically effective amount of two or more overlapping fragments of SEQ ID NO: 1 and a pharmaceutically acceptable carrier, wherein at least one of the polypeptide fragments is antigenic."

"7. The composition of claim 1 or 2, wherein the fragments are about 20 amino acids in length and comprise a first polypeptide fragment and a second polypeptide fragment that overlap by about 10 amino acids."

Claim 1 of the main request and auxiliary request 1 reads (amendments compared with claim 1 of the application as filed highlighted by the board):

"1. A composition comprising a therapeutically effective amount of ~~two or more overlapping fragments~~ 10 fragments of SEQ ID NO: l covering the entire preproinsulin sequence and a pharmaceutically acceptable carrier, wherein ~~at least one of the polypeptide fragments is antigenic~~ the fragments are 20 amino acids in length and are designed such that each following fragment overlaps by 10 amino acids with the preceding fragment."

Claim 1 of auxiliary requests 2 and 3 reads:

"1. A composition comprising a therapeutically effective amount of two or more overlapping fragments of SEQ ID NO: l and a pharmaceutically acceptable carrier, wherein at least one of the polypeptide fragments is antigenic, wherein the fragments are 20 amino acids in length and comprise a first polypeptide fragment and a second polypeptide fragment that overlap by 10 amino acids, wherein the fragments cover the entire preproinsulin sequence."

Claim 1 of auxiliary requests 4 and 5 reads:

"1. A composition comprising a therapeutically effective amount of two or more overlapping fragments of SEQ ID NO: l and a pharmaceutically acceptable carrier, wherein at least one of the polypeptide fragments is antigenic, wherein all the fragments are of a uniform length of 20 amino acids and all the fragments have a uniform overlap of 10 amino acids, and wherein the fragments cover the entire preproinsulin sequence."

Claim 1 of auxiliary request 6 differs from claim 1 of the main request in that it relates to (amendments

compared with claim 1 of the main request highlighted by the board):
"1. A composition ~~comprising~~ consisting of a therapeutically [...]."

Claims 1 and 4 of auxiliary request 8 read:

"1. A composition comprising a therapeutically effective amount of two or more overlapping fragments of SEQ ID NO: l and a pharmaceutically acceptable carrier, wherein at least one of the polypeptide fragments is antigenic, wherein all the fragments are of a uniform length of 20 amino acids and all the fragments have a uniform overlap of 10 amino acids."

"4. A method of making the composition of any one of claims 1-3 comprising combining two or more overlapping fragments of SEQ ID NO: 1 and a pharmaceutically acceptable carrier, wherein at least one of the polypeptide fragments is antigenic, wherein all the fragments are of a uniform length of 20 amino acids and all the fragments have a uniform overlap of 10 amino acids."

VIII. The appellants' arguments may be summarised as follows.

Main request and auxiliary requests 1 and 6

Amendments (Article 123(2) EPC) - claim 1

Claims 1 and 7 and paragraphs [0060] to [0064] of the application as filed provided a suitable basis under Article 123(2) EPC. From paragraph [0061] it was clear that a fragment length of 20 amino acids was preferred. Paragraph [0062] disclosed that a fragment overlap by

10 amino acids was preferred, paragraph [0063] disclosed the combination of a 20-amino-acid fragment length and a 10-amino-acid overlap, and paragraph [0064] stated that the fragments should cover the entire preproinsulin sequence.

Moreover, example 1 (paragraphs [0105] and [0107]) also provided a basis for a fragment length of 20 amino acids with a 10-amino-acid overlap. Reading paragraph [00117] (example 2), a skilled person would immediately understand that the preproinsulin polypeptide vaccine set out in that passage used the preparation as described in example 1. Moreover, a skilled person reading the entire description would have had a clear pointer towards the combination of peptides with a length of 20 amino acids and a 10-amino-acid overlap.

It was evident from reading paragraphs [0070] to [0073] of the application as filed that the peptides should cover the entire preproinsulin sequence. Covering the entire preproinsulin sequence avoided the need to know the relevant epitopes.

Auxiliary requests 2 to 5

Clarity (Article 84 EPC) - claim 1

The skilled person interpreted a claim with a mind willing to understand, so as to arrive at an interpretation which was technically sensible and took account of the whole disclosure of the patent, especially paragraphs [0061], [0062] and [0064] of the application as filed.

Interpreting claim 1 to comprise 10 preproinsulin fragments was the only technically sensible

interpretation as this was the only way to produce fragments with the claimed length and overlap that covered the entire preproinsulin sequence. Any other interpretation would be technically illogical and should thus be excluded. Therefore, the phrasing "two or more" used was redundant in view of the later feature that the fragments must cover the entire preproinsulin sequence.

Auxiliary request 7

Admittance (Article 13(1) RPBA)

The new claim request was aimed at addressing the clarity objections discussed in the context of auxiliary requests 2 to 5. The amendment also addressed the new objection under Article 84 EPC against the series of "and/or" connectors in claim 6 of the previous auxiliary request 7 (as filed on 17 May 2022), which was raised by the board for the first time during the oral proceedings.

Auxiliary request 8

Amendments (Article 123(2) EPC) - independent claims

The basis for amended claim 1 of auxiliary request 8 was found in claims 1 and 7 in combination with paragraphs [0061], [0062] and [00105] of the application as filed.
Claim 4 was based on claim 42 of the application as filed, together with the additional amendments made to claim 1 to make the claims consistent. The basis for these amendments was as explained for claim 1.

IX. *Appellants' requests*

The appellants requested that the decision under appeal be set aside and a patent be granted according to the set of claims of the main request, or, alternatively, according to the set of claims of one of auxiliary requests 1 to 6 (as filed with the statement of grounds of appeal), auxiliary request 7 (as filed during the oral proceedings), auxiliary requests 8 to 12 (as filed by letter dated 17 May 2022) or auxiliary requests 13 and 14 (as filed by letter dated 25 May 2022).

Reasons for the Decision

Main request and auxiliary requests 1 and 6

Amendments (Article 123(2) EPC) - claim 1

1. The passages in the application as filed cited by the appellants do not provide a suitable basis for the claimed subject-matter. Starting from the subject-matter of claim 7 of the application as filed, multiple selections from several options disclosed in paragraphs [0061] to [0064] and examples 1 and 2 of the application as filed are necessary to arrive at the subject-matter of claim 1.

1.1 Dependent claim 7 in combination with independent claim 1 of the application as filed defines the presence of two or more overlapping fragments of preproinsulin (= SEQ ID NO: 1) and specifies that the two or more overlapping fragments are about 20 amino acids in length and that a first and a second polypeptide fragment overlap by about 10 amino acids.

The overlap between the first and second polypeptide fragments is defined as being about 10 amino acids.

1.1.1 A first selection has to be made to arrive at fragments that have a uniform overlap of 10 amino acids not only between a first and a second polypeptide fragment (see paragraph [0062]).

Paragraph [0062] explains that the fragments include a first and a second polypeptide fragment that overlap by about 10 amino acids or alternatively by about 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4 or 3 amino acids. Moreover, it states that "[c]*omposition* [sic] *in accordance with the present invention can include fragments of uniform overlap (e.g., all about 10 amino acids) as well as varying overlap. Again, overlap lengths, or distributions thereof, can be selected to optimize an immunomodulatory effect*". No preference is given as to whether the fragments should have a uniform or a varying overlap.

1.1.2 A second selection has to be made between compositions that include fragments covering the entire preproinsulin sequence and compositions that include fragments limited to a subset of preproinsulin epitopes.

Paragraph [0064] offers the choice between compositions including fragments that either essentially cover the entire preproinsulin sequence or are limited to a set or subset of preproinsulin epitopes. Again, there is no preference for one of the options offered.

1.1.3 Paragraphs [0022], [0026] and [0070] to [0073], cited by the appellants as teaching the vaccine composition and its technical effect according to the invention, do

not provide a direct and unambiguous disclosure of the claimed combination of features either.

1.1.4 "*Example 1 - Polypeptide Synthesis*" provides no pointer since it only relates to the "polypeptide synthesis" and not the vaccine composition. Paragraph [00105], "*Chemistry and Manufacturing Introduction*", states that "[o]*verlapping preproinsulin amino acid peptides are designed such that each of following peptides overlaps by 10 amino acids with the preceding peptide sequence*". However, from this example it cannot be directly and unambiguously derived whether the entire preproinsulin sequence or only part of it is covered.

"*Example 2 - Preproinsulin Polypeptide Vaccine Formulations*" is of no help either since it relates to preproinsulin polypeptide (3P) vaccine formulations A to E, which are a combination of "*the water-soluble preproinsulin 20-amino acid overlapping polypeptide mixture*" and an immunological adjuvant such as different incomplete Freund's adjuvants (A to D) or an immunological adjuvant other than incomplete Freund's adjuvant (E). No information on the number of peptides and the preproinsulin sequence covered by these individual vaccine formulations is provided.

1.2 For want of any indication that the selected parameters are preferred over the others, and of any pointer to the specific combination of features, claim 1 of the main request and auxiliary request 1 contains subject-matter which extends beyond the content of the application as filed (Article 123(2) EPC).

1.3 The same reasons apply *mutatis mutandis* to the subject-matter of claim 1 of auxiliary request 6, which

consequently also extends beyond the content of the application as filed (Article 123(2) EPC).

Auxiliary requests 2 to 5

Clarity (Article 84 EPC) - claim 1

2. The subject-matter of claim 1 of each of auxiliary requests 2 to 5 lacks clarity as per Article 84 EPC since the claims define at least 2 mutually exclusive requirements:

(a) The composition comprises 2 fragments of 20 amino acids in length, the first and second fragment overlapping by 10 amino acids, i.e. leading to a maximum number of 30 amino acids, which is considerably below the 110 amino acids necessary to cover the entire preproinsulin sequence.

(b) The composition (inevitably) comprises more than 2 overlapping fragments of 20 amino acids in length, the first and second (auxiliary requests 2 and 3) or all of them (auxiliary requests 4 and 5) overlapping by 10 amino acids, the fragments covering the entire preproinsulin sequence.

3. The entire preproinsulin sequence consists of 110 amino acids. More than the two claimed fragments of 20 amino acids in length are necessary to cover the entire preproinsulin sequence. For example, if the first and second fragments overlap by 10 amino acids, at least 5 more fragments with an overlap of at least 2 amino acids, i.e. 7 fragments in total, would be necessary to cover the entre preproinsulin sequence.

4. The appellants argued that a skilled person would have immediately recognised that the "two" (i.e. interpretation (a)) was the wrong feature in claim 1. However, this assertion cannot resolve the lack of clarity of claim 1 of these requests.

5. Under established case law (see Case Law of the Boards of Appeal, 9th edition, 2019, II.A.3.1. and II.A. 6.3.5), Article 84 EPC requires that the claims must be clear in themselves when read using normal skills including knowledge of the prior art but not any knowledge derived from the description contained in the patent application.

The wording of claim 1 of auxiliary requests 2 to 5 is rendered unclear by the conflicting requirements of "2 or more fragments of 20 amino acids in length" and "covering the entire preproinsulin sequence". When considered individually, both of these requirements are logical and make technical sense; they are technically meaningful delimitations of the subject-matter claimed. The lack of clarity results from their being combined. On the basis of the wording of the claim alone, it therefore cannot be concluded that the requirement of "two ... fragments of 20 amino acids in length" is erroneous, as argued by the appellants.

Even if a skilled person were to consult paragraphs [0061], [0062] and [0064] of the application as filed (to which the applicants referred) to resolve the conflict, they would still be in doubt as to the definition of the subject-matter for which protection is sought.

Thus, the reference to features explained in the description does not change the board's conclusion on

the clarity of the claims, which results from the wording of the claims alone.

Consequently, claim 1 of each of auxiliary requests 2 to 5 contravenes Article 84 EPC.

Auxiliary request 7

Admittance (Article 13(2) RPBA)

6. Article 13(2) RPBA states that any amendment to a party's appeal case made after the expiry of a period specified by the board in a communication under Rule 100(2) EPC or, where such a communication is not issued, after notification of a summons to oral proceedings is, in principle, not to be taken into account unless there are exceptional circumstances, which have been justified with cogent reasons by the party concerned.

7. The board notes that the objection under Article 84 EPC against the use of multiple "and/or" connectors in several claims of various claim requests had already been raised in the board's communication under Article 15(1) RPBA (see e.g. point 16 or 28).

In reply to this preliminary opinion of the board, the appellants filed 8 auxiliary requests, none of which addressed this objection (see items V. and VI. above). The appellants did not indicate that they had not understood the board's objection.

8. During oral proceedings, the Chairwoman referred to the board's objection concerning the "and/or" connectors and gave one concrete example of incompatible technical features, merely for illustration. Although this

example had not been given in the communication, objectively it could not have come as a surprise. The appellants knew the specific feature objected to and the newly filed sets of claims could have been checked in this regard. Thus, the Chairwoman's example could not have been a surprise, even a subjective surprise.

9. Applicants are responsible for defining the subject-matter claimed. They cannot expect to be assisted in doing so or to have each individual claim of every claim request examined in detail. It is sufficient for applicants to be made aware of an objection and be able to react to it. This does not rule out the possibility of an objection being raised in more general terms against several claim sets, as long as the applicant can be expected to understand that objection. Applicants should therefore not wait for detailed reasoning to examine an objection that has been drafted in more general terms. Rather, they are duty-bound to react within the reasonable time, by either presenting their arguments or filing amended claims, or to check with the board if they do not understand the objection.

As explained above, the appellants should have been able to understand the board's objection raised against the use of multiple "and/or" connectors in several claims of various claim requests even without the example given by the Chairwoman during oral proceedings. This illustration of the board's objection cannot be considered to be a new issue raised by the board during oral proceedings which could qualify as exceptional circumstances. Therefore, auxiliary request 7, filed during oral proceedings, is not admitted into the proceedings (Article 13(2) RPBA).

Auxiliary request 8

Amendments (Article 123(2) EPC) - independent claims 1 and 4

10. The subject-matter of claims 1 and 4 is directly and unambiguously derivable from claims 1 and 7 and from paragraph [00105] of the application as filed, which provides a pointer to using polypeptides of 20 amino acids in length with a 10-amino-acid overlap.

Thus, independent claims 1 and 4 do not contain subject-matter which extends beyond the content of the application as filed (Article 123(2) EPC).

Clarity (Article 84 EPC)

11. The board also considers claims 1 and 4 of auxiliary request 8 to be clear (Article 84 EPC).

Remittal (Article 111 EPC)

12. The decision under appeal did not deal with the subject-matter of the set of claims of auxiliary request 8, which differs considerably from the subject-matter on which the decision under appeal is based. The present decision is limited to assessing the amendments made to independent claims 1 and 4 of auxiliary request 8 and the clarity of those claims.
Pursuant to Article 111(1) EPC, the board decided to remit the case to the examining division for further consideration of the outstanding issues.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the examining division for further prosecution.

The Registrar: The Chairwoman:

I. Aperribay M. Pregetter

Decision electronically authenticated