

I. Summary of Facts and Submissions

- 1 European patent 3 441 466 having the title "METHOD FOR PRODUCING A NOVEL RECOMBINANT FACTOR C, METHOD FOR MITIGATING REACTION INHIBITION IN ENDOTOXIN ASSAYS, AND METHOD FOR MEASURING ENDOTOXIN " is based upon European patent application No. 18 190 686.8 filed on 10-12-2013. It claims priority of JP 2012269840 filed on 10-12-2012.

The mention of the grant of the patent has been published in the European Patent Bulletin of 05-02-2020.

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The Opponent requested revocation of the patent in its entirety based on Article 100(a) EPC for lack of novelty and inventive step under Articles 54 and 56 EPC, respectively, Article 100(b) EPC for lack of sufficiency of disclosure and Article 100(c) EPC for added subject-matter under both Articles 76(1) EPC and 123(2) EPC. D1-D19 were provided as evidence (see Annex I). As an auxiliary measure oral proceedings were requested.

- 3 Further submissions
- 3.1 In a letter received on 18-03-2021, the Proprietor requested the maintenance of the patent in amended form (Article 101(3)a EPC) based on a Main Request or alternatively on Auxiliary Requests 1-2 filed therewith. As an auxiliary measure oral proceedings were requested. D20, D21, D21(I)-(VII), D22 and D23 were submitted as evidence (see Annex I).
- 3.2 On 05-07-2021 the Opposition Division issued a summons to attend oral proceedings on 04-10-2022.

- 3.3 In a letter received on 03-08-2022, the Proprietor requested the maintenance of the patent in amended form (Article 101(3)a EPC) based on a Main Request (MR) or alternatively on Auxiliary Requests AR1-9 filed therewith and replacing the Main and Auxiliary Requests previously on file. As an auxiliary measure oral proceedings were requested. D24 and D25 were submitted as evidence (see Annex I).
- 3.4 In a letter received on 04-08-2022, the Opponent maintained the request for revocation of the patent in its entirety. D26-D35 were submitted as evidence (see Annex I).
- 3.5 In a letter received on 01-09-2022, the Opponent maintained the request for revocation of the patent in its entirety. D26-D55 were submitted as evidence (see Annex I). It was requested not to admit the MR, AR1-AR9 and D24 into the procedure.
- 3.6 On 27-09-2022 the Proprietor maintained the requests filed on 03-08-2022. D56-D61 were submitted as evidence (see Annex).
- 4 On 04-10-2022, oral proceedings were held. Both parties confirmed their requests. In addition, the Proprietor requested not to admit D36-D55 in the proceedings.
- 5 The decision is based on the following requests: see Annex II.

II. Reasons for the decision

6 **Main Request**

6.1 Independent claim 1 reads:

A method for producing a water soluble horseshoe crab Factor C for use in endotoxin assay in the presence of a salt ion, the method comprising:

expressing the horseshoe crab Factor C in a human embryo kidney cell or a Chinese hamster ovary cell as a host cell, wherein the thus-expressed horseshoe crab Factor C is detected in a soluble fraction, and recovering the expressed horseshoe crab Factor C as a solution containing the horseshoe crab Factor C, which is a culture supernatant containing Factor C, wherein the Factor C has activity of Factor C, and contains (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a horseshoe crab Factor C expressed using Sf9 as a host cell, wherein the Factor C exhibits a higher residual activity

~~(i) in the presence of 21 mM sodium citrate, and/or~~

~~(ii) in the presence of 52 mM sodium hydrogencarbonate, and/or~~

~~(iii) in the presence of 214 mM sodium chloride, and/or~~

~~(iv) in the presence of 16 mM magnesium sulfate,~~

as compared with a horseshoe crab Factor C expressed in Sf9 as a host cell, and wherein the activity of Factor C is an activity that the Factor C is activated in the presence of endotoxin to convert Factor B into activated Factor B.

(underlined and strikethrough parts represent the amendments).

6.2 Independent claim 5 reads:

*A method for measuring endotoxin in a test specimen, the method comprising:
a step of mixing an assay agent comprising a horseshoe crab Factor C produced by a human embryo kidney cell or a Chinese hamster ovary cell as a host cell and the test specimen, and a step of measuring the progress of a cascade reaction, wherein the horseshoe crab Factor C has activity of Factor C, contains (α -2,3) linked terminal sialic acid in a greater amount as compared with a horseshoe crab Factor C expressed in Sf9 as a host cell and a native horseshoe crab Factor C, and is recovered as a solution containing the horseshoe crab Factor C, which is a culture supernatant containing Factor C, wherein the test specimen contains sodium ion, ~~and~~ wherein the contained amount of the ion in the test specimen is such an amount that the concentration of the sodium ion derived from the test specimen becomes 20 mM or higher, as a final concentration in the reaction system after mixing the test specimen with the assay agent, and wherein the activity of Factor C is an activity that the Factor C is activated in the presence of endotoxin to convert Factor B into activated Factor B.*

7 **Admissibility**

7.1 The Opposition Division considers that the MR is admissible.

7.2 The Opponent has objected to the admissibility of the MR. The replacement of the request filed on 18-03-2021 by those 03-08-2022 entailed a change of framework of the case and introduced too many new issues. Features had been introduced from the description, which required a completely new search. Additional selections from lists had been introduced to the claims and there were many problems under Art. 84 EPC. The requests were not converging and there was no logical sequence of the requests. Meeting the Rule 116 EPC deadline was not enough.

7.3 The discretion to admit requests into the procedure lies with the Opposition Division. The claims were submitted within the Rule 116 EPC time limit and represented a *bona fide* attempt to overcome the objections presented not only in the notice of opposition but also in the preliminary opinion of the Opposition Division. Their submission left ample time to study the requests, provide counter-evidence and formulate counter-arguments. There are no signs of

procedural abuse. The amendments were occasioned by a ground of opposition under Rule 80 EPC. Whether such an attempt is successful or not, is not a matter to be discussed under admissibility. The stage at which these requests are filed is not so late that the clear allowability criterion (Guidelines H-II, 2.7.1) already has to be applied. This discretionary decision to admit the MR as filed on 03-08-2022 has thus taken into account the relevant facts of the particular case and struck a balance between the interests of the parties in line with the Guidelines E-VI, 2.1 and 2.2.

8 **Article 100(c) EPC in combination with Articles 76(1) and 123(2) EPC**

8.1 The Opposition Division finds that the Main Request does not meet the requirements of Arts. 76(1) EPC and 123(2) EPC, due to the presence of combinations of individualised features selected from multiple lists (both claims 1 and 5) and the presence of the introduction of an undisclosed combination of features. It is to be noted that the description of the earlier application as originally filed (i.e. the parent application) and for the application underlying the present patent (the divisional application for the present patent as filed) are identical. Their claims, however, differ.

8.1.1 In particular, for claim 1 the features (a) "*recovering the expressed horseshoe crab Factor C as a solution containing the horseshoe crab Factor C, which is a culture supernatant containing Factor C*", (b) "*contains (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a horseshoe crab Factor C expressed using Sf9 as a host cell*" and (c) "*wherein the Factor C exhibits a higher residual activity in the presence of 52 mM sodium hydrogencarbonate as compared with a horseshoe crab Factor C expressed in Sf9 as a host cell*", each amount to individualised selections from one or two lists without appropriate basis under Art. 76(1) EPC to combine these selections. Under Art. 123(2) EPC, features (a) and (c) each amount to individualised selections from one or two lists without appropriate basis to combine these selections.

8.1.2 For claim 5, the features (d) "*contains (α -2,3) linked terminal sialic acid in a greater amount as compared with a horseshoe crab Factor C expressed in Sf9 as a host cell and a native horseshoe crab Factor C*", (e) "*and is recovered as a solution containing the horseshoe crab Factor C, which is a culture supernatant containing Factor C*" and (f) "*wherein the test specimen contains sodium ion, wherein the contained amount of the ion in the test specimen is such an amount that the concentration of the sodium ion derived from the test specimen becomes 20 mM or higher, as a final concentration in the reaction system after mixing the test specimen with the assay agent*", each amount to individualised selections from one or two lists without appropriate basis under Art. 76(1) EPC

to combine these selections. Under Art.123(2) EPC, features (d) and (e) each amount to individualised selections from one or two lists without appropriate basis to combine these selections. In addition there is no basis for the "and"-operator in feature (d) under either Article.

- 8.2 The Proprietor has argued that a basis for claim 1 can be found in the description on page 6, paragraph [0016]; page 30, paragraph [0019], in particular page 30, lines 16-17; page 31, paragraph [0022], in particular page 31, lines 26 and 27; and page 32, lines 7 to 10; page 33, paragraphs [0023] and [0024], in particular page 33, lines 2 to 4, 18, and 19; page 36, paragraph [0028], in particular page 36, lines 3-5; page 40, paragraph [0035], in particular page 40, lines 19 to 26; and page 41, lines 13 to 16; page 43, paragraphs [0036] to [0038], in particular page 43, lines 1 to 6, 12 to 22, and 24 to 26; and page 44, lines 7, 8, 12, and 13; page 45, paragraph [0042], in particular page 45, line 26 to page 46, line 4; page 46, paragraph [0043], in particular page 46, lines 23 and 24; and page 71, paragraphs [0099] and [0100], in particular page 71, lines 18 to 23.

The Proprietor has argued that a basis for claim 5 can be found in the description on page 31, paragraph [0022], in-particular page 31, lines 26 and 27; and page32, lines 7 to 10; page 33, paragraphs [0023] and [0024], in particular page 33, lines 2 to 4, 18, and 19; page 43, paragraphs [0037] and [0038], in particular page 43, lines 24 to 26; and page 44, lines 7, 8, 12, and 13; page 45, paragraph [0042]; page 46, paragraph [0043]; page 62, paragraph [0078], in particular page 62, lines 22 to 27; and page 71, paragraph [0100], in particular page 71, lines 22 and 23; and page 72, lines 4 to 16.

Par.0017 had also implicitly been indicated as a basis for both claims by the Proprietor, by indicating that they did not acquiesce to the Opponent's arguments with respect to this paragraph.

- 8.2.1 In particular, addressing the objections under item 8.1.1, feature (a) could be found in par.0042, where it represented a preferred embodiment. It represented the selection of one feature from one list; not an individualised combination from multiple lists. Feature (b) was found in par.0023, where it was stated that the Factor C of the present invention contained sialic acid in a greater amount, as compared with a control Factor C. This control factor C was again indicated in par.0024 including a recombinant Factor C expressed in insect cell Sf9 and a native Factor C . Feature (c) was found in par.0035 and did not involve a selection from two lists in that paragraph. Rather, the higher residual activity in the presence of 52mM sodium hydrogencarbonate was as compared to the control factor C, which control factor C in the same paragraph had been

indicated as including a recombinant Factor C expressed in insect cell Sf9 and a native Factor C. The 52mM sodium hydrogencarbonate was a preferred embodiment as it represented a narrower range in line with T1621/16. This required only one selection, namely of Sf9. In addition reference was made to claim 6 of the application as filed and claim 24 of the earlier application as filed, in which the selections for feature (b) had already been made.

8.2.2 In particular, addressing the objections under item 8.1.2, feature (d) was found in par.0023, where it was stated that the Factor C of the present invention contained sialic acid in a greater amount, as compared with a control Factor C. This control factor C was again indicated in par.0024 including a recombinant Factor C expressed in insect cell Sf9 and a native Factor C. Moreover, here the "and"-operator was used, resolving the other objection under item 8.1.2. Feature (e) could be found in par.0042, where it represented a preferred embodiment. Feature (f) was found in pars.0099 and 0100: Again here was no selection from two lists: the concentration values on page 72, lines 7-16 were understood to apply to each of the earlier mentioned ions, which included sodium. Moreover the range of 20mM or higher was derived from a converging list, so that the principles of T1621/16 applied: The feature was not associated with an undisclosed technical contribution; and the combination was supported by a pointer in the application as filed, namely in example 5, on page 86 and page 87, line 19-page 88 line 2, where values in this range were indicated, as well as in columns 1,4 and 5 of figure 7. Thus it was not an arbitrary selection, but a converging range disclosed in an example which therefore represented a preferred embodiment. In addition reference was made to claim 12 of the application as filed, in which the selections for features (d) and (f) had already been made.

8.3 The Opposition Division does not follow the arguments under items 8.2.1 and 8.2.2 for the following reasons:

8.3.1 With regard to item 8.2.1, it was not disputed that feature (a) represented a selection from a list in par.0042 containing several members i.e. the solution from which the expressed Factor C could be recovered as a solution containing Factor C could be chosen from "a culture broth, a culture supernatant, a disrupted cell extract, a mixture thereof, or the like". It was however argued that this selection represented a preferred embodiment. This argument cannot be followed: culture supernatant is mentioned as one possibility to recover the protein from among several others which are on an equal footing in par.0042. It must be realised that during the discussion for the main request, no pointers

were provided as to why there could be a pointer to this particular embodiment in this list. The adding of this feature therefore gives rise to a first individualised selection from a list.

With regard to feature (b), the control Factor C from Sf9 must be selected in par. 0024 from a recombinant Factor C expressed in insect cell Sf9 and a native Factor C as having a comparative lower sialic acid level. No preference is expressed for a control Factor C from Sf9. This gives rise to a second individualised selection from a list.

Feature (c) itself is the result from two individualising selections: 1) Again the control Factor C from Sf9 must be selected from a recombinant Factor C expressed in insect cell Sf9 and a native Factor C, but now in the framework of a comparative lower residual activity. 2) A higher residual activity in the presence of 52 mM sodium hydrogencarbonate is selected from multiple values in par.0035. No preference for a control Factor C from Sf9 is expressed in this passage and no particular preference for the 52 mM sodium hydrogencarbonate. Even if the 52 mM appears as a value in a converging set of ranges for salt ions, it is certainly not the most preferred value in this set of values; worse, it is not even a set of ranges and it does not even pertain to the same salt, and therefore they cannot be considered as a set of converging ranges for the same salt ion. The principle of T1621/16 therefore does not apply at all. In fact sodium hydrogen carbonate is an arbitrary selection from a wide variety of types of ions, each associated with a different type of salt, involving different cations and different anions. Therefore, feature (c) gives rise to a third and fourth individualised selection, each from a separate list.

As a consequence, the subject-matter of claim 1, is a combination of multiple individualised selections from multiple lists for which no pointers can be found. The result is patch-worked subject-matter which cannot directly and unambiguously be derived from the application as filed or from the earlier application as filed, contrary to Articles 123(2) EPC and 76(1)EPC, respectively.

Under Article 123(2)EPC, it is immaterial that claim 6 of the application as originally filed already makes a selection for feature (b), since it does not do so for features (a) and (c) and thereby still amounts to a combination of multiple individualised selections from multiple lists for which no pointers can be found.

Under Article 76(1) EPC the assertion that claim 24 of the earlier application as filed already made the selection for feature (b), does not mean that no individualising selection from a list has been made, because the other

alternative in which the amount of sialic acid is compared with natural factor C is in claim 23, which is on an equal footing with claim 24, as both depend on claim 22 of the earlier application as filed.

As the Proprietor did not provide a substantiated explanation as to par.0017 as a basis for the Main Request, this implied argument cannot be taken into account under the *ratio decidendi*, however it will be discussed as an *obiter dictum* below.

Obiter dictum in the framework of item 8.3.1:

As the Opponent has briefly made reference to par.0017 as a potential basis, the following considerations apply:

Par. 0017 is what is called a set of "claim-like clauses" (Guidelines FIV, 4.4). It comprises 6 different aspects [1]-[6], for each of which further embodiments have been indicated. However, even if these embodiments try to refer to all of the above described entities or activities, it is not unambiguous if such a reference is to the highest aspect level numbered [1]-[6] or also to the subsection embodiments belonging to these aspects. Some of these embodiments are at the same level of granularity in this numbering system and are alternatives of each other, which cannot be used in combination without technical contradictions. Therefore the reference system in this paragraph which perhaps tries to connect all these embodiments and/or aspects without having given it a second thought, cannot be taken serious. It should be remembered that the content of an application cannot and must not be considered to be a reservoir from which features pertaining to separate embodiments of the application can be combined in order to artificially create a particular embodiment (Guidelines H-V.3.2.1).

Furthermore, when considering these alternatives, to arrive at some of the claimed subject-matter, still multiple individualising selections must be made without there being a pointer as to why they can be combined.

In more detail, subsection [2] of par.0017 refers to *A method for producing a water soluble horseshoe crab Factor C*, which is also the beginning of the preamble of present claim 1. This section is silent on features (a),(b) and (c) discussed above.

In subsection [3], which refers to a product-per-se, namely "*A horseshoe crab Factor C producible by the above-described method*", there are certain features which appear to correspond with features (a),(b) and (c), but it must be carefully

assessed, whether they really are identical and implied in the framework of the method of subsection [2] and whether they do or do not involve an individualising selection from a list of alternatives on the same footing.

For feature (a) the stipulation in subsection [3.7] of par.0017 "The above-described Factor C, which is a culture supernatant containing Factor C" is not co-extensive in meaning with "*recovering the expressed horseshoe crab Factor C as a solution containing the horseshoe crab Factor C, which is a culture supernatant containing Factor C*". After all, recovering as a solution requires that the culture supernatant is *de facto* separated from cellular debris and other precipitates, which is not necessarily the case in product-per-se item [3.7] in par.0017.

Moreover, for feature (b) item [3.2.4] must be selected from a list of alternatives on an equal footing comprising [3.2.3] and [3.2.4] and for feature (c) item [3.3.12] must be selected from a list of alternatives on an equal footing comprising items [3.3.11] - [3.3.15]. There's no pointer indicating they can be combined. Therefore, also from par.0017 no appropriate basis can be obtained for claim 1 under Art. 76(1) EPC and Art.123(2) EPC.

- 8.3.2 With regard to item 8.2.2, with regard to feature (d), the indicated basis for the "and"-operator in claim 5 between "*a horseshoe crab Factor C expressed in Sf9 as a host cell*" and "*a native horseshoe crab Factor C*" is flawed: Whenever the comparison of sialic acid levels is at stake, the application speaks of "a Factor C" or "the Factor C" i.e. in the singular form. The passage in the first lines of par.0024 stating "*Examples of the control Factor C include a recombinant Factor C expressed in insect cell Sf9, and a native Factor C*" should not be misconstrued. It refers again to "the control Factor C" i.e. a single type. The "**and**"-operator in this passage shows the two types of examples that are available for such a single type of Factor C, but does not imply that they can or should be used together. Even if the interpretation of the opponent of the "and"-operator in this passage were ambiguous, then still there would be multiple possibilities to choose from, namely 1) a single recombinant Factor C expressed in insect cell Sf9, 2) a single native Factor C and 3) a combination of both. Therefore, feature (d) has no appropriate basis.

As regards feature (e), for the same reasons as above under item 8.3.1, the argument that this selection represented a preferred embodiment cannot be followed: culture supernatant is mentioned as one possibility to recover the protein from among several others which are on an equal footing in par.0042. It

must be realised that during the discussion for the main request, no pointers were provided as to why there could be a pointer to this particular embodiment in this list. This gives rise to a individualised selection from a list.

As regards feature (f) even if it is conceded that the concentration ranges on page 72, lines 7-16 were understood to apply to each of the earlier mentioned ions, which included sodium, then still the combination of sodium as ion derived from the test specimen and the 20 mM or higher range together constitutes an individualised selection from a list. It is then immaterial that the 20 mM or higher range comes from a converging list, because that list then also contains the combination of the range of "20mM or higher" for the ions of potassium, calcium and magnesium. Moreover, even if the 20 mM or higher appears as a range in a converging set of ranges for salt ions, it is certainly not the most preferred value in this set of ranges. In addition T1621/16 requires that the combination should be supported by a pointer. The pointer indicated by the applicant in example 5, on page 86 and page 87, line 19-page 88 line 2, where values in this range were indicated as well as in columns 1,4 and 5 of figure 7, does not convincingly point to this particular range when compared to the even more preferred ranges of "50mM or higher" and "100mM" on page 72, lines 7-16. After all, page 87, line 19-page 88 line 2 also mentions values of 52mM, 77mM and 214 mM when the cation is sodium. These values are also reflected in figure 7. It is therefore not accepted that the skilled person would contemplate this particular less preferred range of 20mM or higher for sodium as ion derived from the test specimen when there are other more preferable selections available. Therefore the inclusion of feature (f) gives rise to another individualised selection from a list.

As a consequence, part of the subject-matter of claim 5, is a combination of multiple individualised selections from multiple lists for which no pointers can be found. Part of the subject-matter of claim 5 relates to an embodiment with no basis at all. The result is patch-worked subject-matter which cannot directly and unambiguously be derived from the earlier application as filed, contrary to the provisions of Art. 76(1) EPC.

The assertion that claim 12 of the application as filed already provides selection for features (d) is also not correct: In claim 12 of the application as filed the (α -2,3) linked terminal sialic acid is required to be present in a greater amount as compared with a horseshoe crab Factor C expressed in Sf9 as a host cell alone; not as compared with a horseshoe crab Factor C expressed in Sf9 as a host cell and compared with a native horseshoe crab Factor C. As explained above, the "and"-operator does not have a basis (neither in the application as

filed nor in the earlier application as filed) and even if the possibility were present by virtue of ambiguity, it would represent yet a further individualised selection. Therefore also under Article 123(2) EPC claim 5 fails to meet the requirements.

Obiter dictum in the framework of item 8.3.2:

As the Opponent has briefly made reference to par.0017 as a potential basis, the following considerations apply in analogy to what has been explained about this paragraph under item 8.3.1:

In more detail, subsection [6] of par.0017 refers to, which is also the beginning of the preamble of present claim 5.

Feature (f) can be arrived at only via two individualising selections in this section: sodium [6.2.2] is selected from a list of alternatives on an equal footing in subsections [6.2.2]-[6.2.5] and the "20mM or higher" range is selected from a list of alternatives in subsections [6.6.1]-[6.6.7]. If one were to apply the convergence doctrine of T1621/16, then still [6.6.6]-[6.6.7] are more preferred than the "20mM or higher" range in subsection [6.6.5], so that there's no reason or pointer to select exactly this less preferred one.

Feature (d) cannot be imported from section [3] of par.0017 as there's no disclosure there of sialylation compared to both a horseshoe crab Factor C expressed in Sf9 as a host cell and a native Factor C. If it could, it would amount to yet a further individualised selection.

There's no pointer indicating these individualised selections can be combined.

Therefore, also from par.0017 no appropriate basis can be obtained for claim 5 under Art. 76(1) EPC and Art.123(2) EPC.

9 **Auxiliary Request 1 (AR1)**

9.1 AR1 contains only one independent claim (i.e. claim 1), which is identical to claim 1 of the MR.

10 **Admissibility**

10.1 The Opposition Division considers that AR1 is admissible.

10.2 The Opponent has objected to the admissibility of the AR1 for the same reasons as for the MR. In addition, it was stated that since there were claims that *prima facie* did not overcome the objections, the request should not be admitted into the procedure.

10.3 The Opposition Division traverses with this opinion for the same reasons as under item 7.3.

11 **Article 100(c) EPC in combination with Articles 76(1) and 123(2) EPC**

- 11.1 The Opposition Division finds that AR1 does not meet the requirements of Arts. 76(1) EPC and 123(2) EPC.
- 11.2 The Proprietor submitted that no further arguments were submitted, implying that the arguments presented in writing and presented during the oral procedure for the MR applied *mutatis mutandis* to AR1.
- 11.3 The Opposition Division does not follow the arguments of the Proprietor, because claim 1 is identical to claim 1 of the MR and the reasons presented for claim 1 of the MR under item 8 apply *mutatis mutandis* to claim 1 of AR1.

12 **Auxiliary Request 2 (AR2)**

- 12.1 Independent claim 1 reads:

A method for producing a water soluble horseshoe crab Factor C for use in endotoxin assay in the presence of a salt ion, the method comprising:

expressing the horseshoe crab Factor C in a human embryo kidney cell or a Chinese hamster ovary cell as a host cell, wherein the thus-expressed horseshoe crab Factor C is detected in a soluble fraction, and recovering the expressed horseshoe crab Factor C as a solution containing the horseshoe crab Factor C, which is a culture supernatant containing Factor C, wherein the Factor C has activity of Factor C, and contains (α -2,3)-linked terminal sialic acid in a greater amount, as compared with a horseshoe crab Factor C expressed using Sf9 as a host cell and a native horseshoe crab Factor C, wherein the Factor C exhibits a higher residual activity in the presence of 52 mM sodium hydrogencarbonate as compared with a horseshoe crab Factor C expressed in Sf9 as a host cell and a native horseshoe crab Factor C, and wherein the activity of Factor C is an activity that the Factor C is activated in the presence of endotoxin to convert Factor B into activated Factor B.

(underlined parts represent the amendments over the MR).

13 **Admissibility**

- 13.1 The Opposition Division considers that AR2 is admissible.
- 13.2 The Opponent has objected to the admissibility of the AR2 for the same reasons as for the MR and AR1. In addition, the situation was aggravated because the problem of the "and"-operator in claim 5 of the MR for which there was no basis had also been introduced in claim 1 of AR2.
- 13.3 The Opposition Division traverses with this opinion for the same reasons as under item 7.3

14 **Article 100(c) EPC in combination with Articles 76(1) and 123(2) EPC**

14.1 The Opposition Division finds that AR2 does not meet the requirements of Arts. 76(1) EPC and 123(2) EPC.

14.2 The Proprietor has argued that there were less selections to be made in AR2 than in the MR, because a comparison to a horseshoe crab Factor C expressed using Sf9 as a host cell did not have to be made for features (b) and (c) as mentioned under item 8.1.1. This was so in view of the now added additional comparison to a native horseshoe crab Factor C in both instances. Moreover, the "and"-operator was warranted by par.0024, first two lines. The addition of feature (a) was warranted because it was preferred in view of the examples and par.0017, page 20, item [3.7] in conjunction with item [2] on page 12.

14.3 The Opponent objected to the introduction of these arguments, as the issues they related to had already been discussed in the framework of the MR.

14.4 Firstly, the Opposition Division considers that in any case there is no basis for the introduction of "and a native horseshoe crab Factor C" in the framework of a comparison of the sialic acid levels. As explained under item 8.3.1 par.0024 fails to provide that basis in the framework of a comparison of the sialic acid levels. In the framework of the comparison of residual activity, this basis is also flawed for the introduction of "and a native horseshoe crab Factor C", as par.0024 is altogether silent on residual activity.

Secondly, as regards the assertion that item [3.7] in conjunction with item [2] in par.0017 provides a basis or pointer for feature (a) as mentioned under item 8.1.1, the stipulation in product-per-se related subsection [3.7] of par.0017 i.e. "*The above-described Factor C, which is a culture supernatant containing Factor C*" is not co-extensive in meaning with the method step of "recovering the expressed horseshoe crab Factor C as a solution containing the horseshoe crab Factor C, which is a culture supernatant containing Factor C". It also does not necessarily imply this: after all, recovering as a solution requires that the culture supernatant is *de facto* separated from cellular debris and other precipitates, which is not necessarily the case in product-per-se item [3.7] in par.0017. As such subsection 3.7 buried in a long list of embodiments and aspects does not provide a pointer either. It should be remembered that the content of an application cannot and must not be considered to be a reservoir from which features pertaining to separate embodiments of the application could be combined in order to artificially create a particular embodiment (Guidelines H-V. 3.2.1).

Thirdly, although in the examples a culture supernatant is recovered, this is not the end of the story: after this step the supernatant is filtrated (see pars. 0107,0113 and 0121) and only the thus-recovered fraction (i.e. the filtrate) was employed as recombinant horseshoe crab Factor C in section "4. Activity measurement" of the examples. In other words it is the horseshoe crab Factor C in the filtrate, that according to the examples qualifies as "*a water soluble horseshoe crab Factor C for use in endotoxin assay in the presence of a salt ion*". This means that feature (a) cannot be extracted from the examples without resulting in an intermediate generalisation, because the feature is *de facto* inextricably linked to another feature of the examples (namely the filtration) and the overall disclosure does not justify the generalising isolation of the feature and its introduction into claim 1. The examples can therefore not provide a pointer for the introduction of culture supernatant without mentioning a subsequent step of filtration.

The Opposition Division thus concludes that there's no basis for the introduction of "*and a native horseshoe crab Factor C*" under both Articles 76(1) EPC and 123(2) EPC, neither in the framework of the comparison of the sialic acid levels nor in the framework of the comparison of the residual activity.

Furthermore, claim 1 still contains combinations of individualised features (a) and (c) as selected from multiple lists, contrary to both Articles 76(1) EPC and 123(2) EPC.

As regards the Opponent's objection concerning the admissibility of the introduction of these further arguments by the Proprietor, the Opposition Division considers that they had to be admitted, because there's no principle in the EPC that further arguments cannot be admitted. Moreover, the framework of the claim had changed a bit, so that it was not automatic that each and every reason previously presented for the MR would apply *mutatis mutandis*. Therefore the Opposition division decided to admit these arguments into the procedure for AR2, although of course they have not been taken into account for the *ratio decidendi* for the MR, which had already been decided on.

Obiter dictum in the framework of item 14.4:

It is noted that subsection [3.3.12] of par.0017 refers to "*The above-described Factor C, which exhibits a higher residual activity in the presence of 52 mM sodium hydrogencarbonate, as compared with a horseshoe crab Factor C expressed in Sf9 as a host cell and/or a native Factor C*". Although the "and"-operator is present here in the framework of the comparison of residual activities, so is the "or" operator, which makes that the choice of the "and"-operator here still amounts to an individualised selection from a list, which causes

problems in combining it with the selections made for features (a) and (c). Therefore this passage cannot remedy the absence of compliance with Articles 76(1) and 123(2) EPC for that part of the claim either.

15 **Auxiliary Request 3-9 (AR3-AR9)**

- 15.1 The wording of the independent claims of AR3-AR9 is presented in Annex III.
- 15.2 Claim 1 of AR3 is based on claim 1 of the MR/AR1, wherein the subject-matter of dependent claim 3 has been incorporated into claim 1.
- 15.3 Claim 1 of AR4 is based on claim 1 of AR2, wherein the subject-matter of dependent claim 3 has been incorporated into claim 1.
- 15.4 Claim 1 of AR5 is based on claim 1 of AR2, wherein the subject-matter of claim 1 has been further limited to refer to HEK293 and CHO-DG44 cells.
- 15.5 Claim 1 of AR6 is based on claim 1 of AR5, wherein the subject-matter of dependent claim 3 has been incorporated into claim 1.
- 15.6 Claim 1 of AR7 is based on claim 1 of the MR/AR1, wherein the subject-matter of claim 1 has been further limited to refer to CHO cells as host cells solely.
- 15.7 Claim 1 of AR8 is based on claim 1 of the AR7, wherein the subject-matter of dependent claim 3 has been incorporated into claim 1. In addition the comparison for the sialic acid levels and residual activity have both been amended to include a comparison to a native horseshoe factor C.
- 15.8 Claim 1 of AR9 is based on claim 1 of the MR/AR1, wherein the subject-matter of claim 1 has been further limited to refer to human embryo kidney cells as host cells solely. In addition, the comparison for the sialic acid levels and residual activity have both been amended to include a comparison to a native horseshoe factor C. Furthermore, the subject-matter of dependent claim 3 has been incorporated into claim 1.

16 **Admissibility**

- 16.1 The Opposition Division considers that AR3-AR9 are admissible.
- 16.2 The Opponent has objected to the admissibility of the AR3-AR9 for the same reasons as for the higher ranking requests.
- 16.3 The Opposition Division traverses with this opinion for the same reasons as under item 7.3.

17 **Article 100(c) EPC in combination with Articles 76(1) and 123(2) EPC**

- 17.1 The Opposition Division finds that AR3-AR9 do not meet the requirements of Arts. 76(1) EPC and 123(2) EPC.

- 17.2 The Proprietor submitted that the arguments presented in writing and presented during the oral procedure for the higher ranking requests applied *mutatis mutandis* to AR3-9.
- 17.3 The Opposition Division does not follow the arguments of the Proprietor for the following reasons:
- 17.3.1 The reasons presented for the MR under item 8 apply *mutatis mutandis* to AR3 and AR7-AR9. The addition of further features from dependent claims or limitation of the type of host cells cannot remedy the flaws presented for the MR under item 8. In fact the limitation to a single type of host cell in AR7 and 9 aggravates the problem as it introduces yet a further individualised selection from a list, which cannot be combined with the individualised selections already in the claim without infringing Articles 76(1) and 123(2) EPC. For claim 8 the addition of a comparison to a native horseshoe factor C for both the sialic acid levels and the residual activity is objected to under Articles 76(1) and 123(2) EPC for the reasons as presented under item 14.4, which apply *mutatis mutandis*.
- 17.3.2 The reasons presented for AR2 under item 14 apply *mutatis mutandis* to AR4-AR6. The addition of further features from dependent claims or limitations of the type of host cells cannot remedy the flaws presented for the AR2 under item 14.

III. Decision

- 18 Regarding admissibility of the requests, the MR and AR1-AR9 are admitted into the procedure.
- 19 As none of the requests (MR and AR1-AR9) meets the requirements of Articles 76(1) EPC and 123(2) EPC, the Patent is revoked pursuant to Article 101(3)b EPC.