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Datasheet for the decision of 24 January 2020

Case Number: T 1471/16 - 3.3.08

Application Number: 13184202.3

Publication Number: 2674487

IPC: C12N9/26

Language of the proceedings: EN

Title of invention:
Large-scale production of soluble hyaluronidase

Applicant:
Halozyme, Inc.

Headword:
Hyaluronidase/HALOZYME

Relevant legal provisions:
EPC Art. 76(1), 83, 84, 54, 56, 123(2)
RPBA 2020 Art. 13

Keyword:
Main request - admission (yes);
Main request - fulfils all requirements of the EPC (yes);

Decisions cited:
T 0080/96, T 0688/14

Catchword:

Europäisches Patentamt
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Beschwerdekammern

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Case Number: T 1471/16 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 24 January 2020

Appellant: (Applicant)	Halozyme, Inc. 11388 Sorrento Valley Road San Diego, CA 92121 (US)
Representative:	Ogle, James Mattew Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 1 February 2016 refusing European patent application No. 13184202.3 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	B. Stolz
Members:	P. Julià
	D. Rogers

Summary of Facts and Submissions

I. European patent application no. 13 184 202.3 (published as EP 2 674 487; hereinafter "the patent application"), a divisional application of the earlier European patent application no. 09 718 114.3 (published under the PCT as International patent application WO 2009/111066; hereinafter "the earlier patent application"), was refused by an examining division of the EPO.

II. The basis for the decision of the examining division was a main request and auxiliary request I to IV. The main request had six claims; claims 1 and 2 read as follows:

"1. A harvested cell culture fluid, comprising soluble recombinant human PH20 (rHuPH20) with an enzymatic activity that is greater than 5000 units of hyaluronidase activity/mL of cell culture fluid as harvested, wherein:

soluble rHuPH20 is a soluble form of human PH20 that is recombinantly expressed in Chinese Hamster Ovary (CHO) cells; and

the harvested cell culture fluid is the fluid as separated from cells, cell debris and aggregates.

2. The harvested cell culture fluid of claim 1, wherein the enzymatic activity is 10,000, 12,000, 14,000, 16,000, 18,000, 20,000, 22,000 or 24,000 units/mL."

III. The main request was considered to lack novelty over document (1) (US 2004/0268425) and not to be inventive. The objections raised against the main request applied *mutatis mutandis* to auxiliary requests I, II and IV;

auxiliary request III lacked only an inventive step. As *obiter dicta*, the examining division stated that all requests contravened Article 123(2) EPC and did not fulfil the requirements of Article 83 EPC.

IV. With the statement setting out its grounds of appeal, the appellant filed a new main request and new auxiliary requests 1 to 4. As an auxiliary measure, oral proceedings were requested.

V. In a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA 2007), the appellant was informed of the board's provisional opinion on the issues of the case.

VI. In reply thereto, the appellant filed new documentary evidence and auxiliary requests 1 to 7 to replace its former auxiliary requests.

VII. Oral proceedings were held on 24 January 2020. At these proceedings, the appellant withdrew its main request and filed a new main request.

VIII. The main request had four claims; claims 1 and 3 read as follows:

"1. A harvested cell culture fluid, comprising soluble recombinant human PH20 (rHuPH20) with an enzymatic activity that is greater than 5000 and less than or equal to 18,000 units of hyaluronidase activity/mL of cell culture fluid as harvested, wherein:

soluble rHuPH20 is a soluble form of human PH20 that is recombinantly expressed in Chinese Hamster Ovary (CHO) cells;

the amino acid sequence of the rHuPH20 encoded by the cells comprises a polypeptide whose sequence is set forth in SEQ ID NO:4 or variants thereof that have 96% or more sequence identity with SEQ ID NO:4, wherein sequence identity is determined over the length of the whole sequence;

a unit of hyaluronidase activity can be determined by incubating soluble rHuPH20 with sodium hyaluronate (hyaluronic acid) for a set period of time (10 minutes), precipitating the undigested sodium hyaluronate with the addition of acidified serum albumin, measuring the turbidity of the resulting sample at 640 nm after a 30 minute development period, and comparing with a calibration curve generated with dilutions of a soluble rHuPH20 assay working reference standard; and

the harvested cell culture fluid is the fluid as separated from cells, cell debris and aggregates.

3. The harvested cell culture fluid of claim 1 or claim 2, wherein the enzymatic activity is 10,000, 12,000, 14,000, 16,000 or 18,000 units/mL."

IX. The submissions of the appellant, insofar as relevant to this decision, may be summarised as follows:

Main request

Admission into the appeal proceedings

The main request addressed the objections raised under Articles 123(2) and 83 EPC by the examining division and those raised by the board in its communication.

Articles 76(1) and 123(2) EPC

The range of hyaluronidase activity in claim 1 was based on a combination of the lower value of the open-range disclosed in paragraph [0011] of the patent application (paragraph bridging pages 5 and 6 of the earlier patent application) with one of the specific activities disclosed therein. The basis for active soluble rHuPH20 variants having 96% or more sequence identity with SEQ ID NO: 4 was the disclosure in paragraph [0017] of the patent application (page 8, lines 29 to 31 of the earlier patent application). The method for determination of the enzymatic activity of soluble rHuPH20 was described in Example 9.

Articles 84 and 83 EPC

Claim 1 required the harvested cell culture fluid (HCCF) to be "as harvested" and "as separated from cells, cell debris and aggregates". The term "as" in these sentences could not be ignored; it was relevant and contributed to a technically meaningful limitation of the claim. In line with the whole disclosure of the patent application, this wording indicated that the claimed HCCF had undergone no further treatment after being "harvested" and "separated from cells, cell debris and aggregates". It excluded the treatment of the HCCF ("as harvested") by any further method-step, such as a concentration step, before activity measurement. The scope of claim 1 did not comprise a concentrated HCCF, which was distinct from the claimed HCCF. The disclosure of the patent application was addressed to a skilled person with common general knowledge in the field, who could know the (natural) composition of a HCCF "as harvested" and assess whether or not it had undergone further treatment.

Although the highest activity of the exemplified HCCF "as harvested" was 17.000 units/mL (Example 8.A, page 47 of the patent application), the range of hyaluronidase activity defined in claim 1, in particular the upper-limit of 18.000 units/mL, was within the normal/standard cell culture variation and it did not require undue burden to, or an inventive contribution from, a skilled person.

Article 54 EPC

Document (1) did not disclose a HCCF "as harvested" and "as separated from cells, cell debris and aggregates" (i.e. a non-concentrated, clarified HCCF) with an activity of soluble rHuHP20 greater than 5.000 units/mL as required by claim 1. Example 8 of this document described a HCCF with a lower concentration of soluble rHuHP20, the highest amount being of 1.600 units/mL. The high amount of hyaluronidase in the HCCF disclosed in the patent application reflected the amount produced by each CHO host cell and showed a significant increase compared to the prior art.

Unlike the pharmaceutical compositions of the claims underlying decision T 80/96 (OJ EPO 2000, 50), the claimed HCCF was not formed by adding something to a soluble rHuHP20. The HCCF was a starting material for purifying soluble rHuHP20 and it was thus the opposite of a pharmaceutical composition formed by adding a buffered composition to an active molecule.

Article 56 EPC

The closest prior art document (1) taught that the final hyaluronidase activity in a culture medium of

DG44 CHO cells transfected with an expression vector encoding a soluble rHuHP20 was 1.600 units/mL (Example 8); this was the starting material for concentration and purification of the soluble rHuHP20 (Example 9). Starting therefrom, the objective technical problem was the provision of an improved starting (HCCF) material for purification of soluble rHuHP20. The higher soluble rHuHP20 output in the HCCF described in Examples 4 to 8 of the patent application reflected a higher output of each recombinant CHO host cell compared to the CHO host cells described in document (1) and showed that the problem was solved. Document (1) did not suggest any method for increasing the production of soluble rHuHP20 and obtaining thereby a clarified HCCF that contained such a high concentration of soluble rHuHP20.

The expression vectors used to transfect the DG44 CHO cells described in Example 8 of document (1) comprised the strong cytomegalovirus (CMV) promoter. A skilled person would not have expected increased amounts of soluble rHuHP20 by using other strong promoters. The technical problem was not solved by the addition of purified hyaluronidase to the HCCF described in document (1). There was no suggestion in document (1) to carry out such addition and the skilled person would not have done it because clarified HCCF was normally used as the starting material for purifying soluble rHuHP20. The concentration of HCCF did not result in the claimed HCCF because it increased the concentration of all molecules in the fluid, including proteins; the background concentration/activity of other proteins in a concentrated HCCF was higher than in the claimed clarified HCCF. The concentration of HCCF did not solve the problem because the production of soluble rHuHP20 per recombinant CHO host cell was not increased. There

was no evidence on file to show that any of the alternatives cited by the examining division or any other alternative derivable from the prior art would have provided the skilled person with a reasonable expectation of success, i.e. achieving the claimed clarified HCCF comprising a soluble rHuHP20 with an activity falling within the range defined in claim 1.

X. The appellant (applicant) requested that the decision under appeal be set aside and that a patent be granted upon the basis of the main request filed at the oral proceedings on 24 January 2020 or, alternatively, upon the basis of one of auxiliary requests 1 to 7 filed under cover of a letter dated 22 January 2020.

Reasons for the Decision

Admission of the main request

1. The main request, filed by the appellant at the oral proceedings before the board, is based on the main and auxiliary requests filed with the statement of grounds of appeal. Compared with the requests underlying the decision under appeal, these requests were amended in order to overcome an objection under Article 123(2) EPC raised by the examining division in its *obiter dicta* but not at earlier stages of the examination proceedings. The main request is also based on the requests filed by the appellant in reply to the board's communication pursuant to Article 15(1) RPBA 2007. The amendments introduced into the main request are straightforward in nature, do not increase the complexity of the case and contribute to procedural efficiency.

2. Therefore, the main request is admitted into the appeal proceedings (Article 13(1) RPBA 2020).

Main request
Articles 76(1) and 123(2) EPC

3. The soluble rHuHP20 variants referred to in claim 1 are defined by having "96% or more sequence identity" with the amino acid sequence as set forth in SEQ ID NO: 4 over the length of the whole sequence. Basis for this subject-matter is found in paragraph [0017] of the patent application (page 8, lines 29 to 31 of the earlier patent application).

4. Paragraph [0011] of the patent application (paragraph bridging pages 5 and 6 of the earlier patent application) discloses an (upper-end) open-range for the hyaluronidase activity comprised in the harvested cell culture fluid (HCCF), namely "an enzymatic activity of greater than 5.000 units/mL". In the same sentence, the specific activities of "such as 10.000, 12.000, 14.000, 16.000, 18.000, 20.000, 22.000 or 24.000 units/mL" are disclosed. In line with the case law (cf. "Case Law of the Boards of Appeal of the EPO", 9th edition 2019, II.E.1.5.2, 455), the combination of the lower-end value of the open-range (5.000 units/mL) with one of the exemplified specific activities falling within this range provides a basis for the closed-range ("greater than 5.000 and less than or equal to 18.000 units of hyaluronidase activity/mL") mentioned in claim 1.

5. A definition of HCCF is found in paragraph [0027] of the patent application (page 10, lines 12 to 17 of the earlier patent application). A more detailed disclosure is given in paragraph [0147] of the patent application

(page 50, lines 7 to 24 of the earlier patent application). The method for the determination of the enzymatic activity of soluble rHuPH20 is described in Example 9 of the patent application and the earlier patent application. This Example provides the basis for the definition of the enzyme activity in claim 1.

6. The subject-matter of dependent claims 2 to 4 (soluble rHuHP20 encoded by cells comprising a polypeptide whose sequence is set forth in any of SEQ ID NOs.: 4 to 9, claim 2; specific activities of "10.000, 12.000, 14.000, 16.000 or 18.000 units/mL", claim 3; use of DG44 CHO cells, claim 4) was not objected to by the examining division under any of Articles 76(1) or 123(2) EPC, nor does the board see any reason to raise an objection of its own motion.

7. Thus, the main request does not contravene Articles 76(1) and 123(2) EPC.

Articles 84 and 83 EPC

8. Claim 1 is directed to a HCCF defined by reference to several features. Some of them are directly related to the method of production of said HCCF, such as the "cell fluid **as** harvested" and "the fluid **as** separated from cells, cell debris and aggregates" (emphasis by the board). The board shares appellant's view that the term "as" in these sentences has a significant technical meaning in the definition of the claimed HCCF because it delimits the claimed subject-matter from harvested cell culture fluid prepared by further method-steps such as the concentration of the HCCF once separated (i.e. clarified) from cells, cell debris and aggregates. The definition of the claimed clarified HCCF is further limited by reference to the method of

production, namely the requirement that the "soluble form of human PH20 is recombinantly expressed in Chinese Hamster Ovary (CHO) cells". Therefore, the claimed clarified HCCF is defined by method-features and, in this sense, it is a product-by-process claim.

9. The claimed HCCF is further defined by reference to functional (range of hyaluronidase activity) and structural (SEQ ID NO: 4) properties of the soluble rHuHP20 comprised in said HCCF. Moreover, since the range of hyaluronidase activity defined in claim 1 is an essential feature of the claimed product, the method of determination of hyaluronidase activity, as described in Example 9 of the patent application, is explicitly mentioned in the claim.

10. In the board's view, the combination of features related to the method of production of the HCCF with the structural and functional features of the relevant component comprised in said HCCF, i.e. the soluble rHuHP20, define the claimed HCCF in a clear and unambiguous manner. In view of the whole content of the patent application, the claimed HCCF is seen as an intermediate product for use in the further purification of soluble rHuHP20. Taking into account the large number of possible cell culture media and culture conditions, the definition of such an intermediate product by a combination of features related to the method of production with (functional and structural) features of the relevant component comprised in said product is considered to be fair and appropriate by the board and in line with the case law (cf. "Case Law", *supra*, II.A.7.3, 318).

11. Examples 4 to 8 of the patent application disclose the culture of several host cell lines - derived from

DG44 CHO cells transfected with an expression vector comprising a nucleic acid encoding soluble rHuPH20 (Examples 1 to 3 of the patent application) - in several cell culture media and under various conditions (bioreactor volumes, with/without feeds, feed compositions, etc.). The resulting clarified harvested cell culture fluids comprise soluble rHuHP20 with hyaluronidase activities falling within the range defined in claim 1 (cf. Tables 13 to 15, 18, 20, 22 and 24 of the patent application). Although the highest hyaluronidase activity reported in these examples is 17.000 units/mL (cf. page 47, lines 52 and 53; Example 8 of the patent application), the board is convinced that, in the light of the technical teaching provided by the patent application, a skilled person can obtain a clarified HCCF with the upper-limit activity (18.000 units/mL) without undue burden or the exercise of inventive skill; the necessary increase falls within the levels of variation usually observed when changing the cell culture media and culture conditions.

12. Therefore, the main request fulfils the requirements of Articles 84 and 83 EPC.

Article 54 EPC

13. Document (1) (US 2004/0268425; publication date: 30 December 2004) is the sole document cited under Article 54 EPC. One of the inventors of this document (L.H. Bookbinder) is also an inventor of the patent application and the disclosure of document (1) is closely related to that of the patent application. Indeed, document (1) is also concerned with the production of soluble rHuHP20 using CHO cells derived from the DG44 CHO cell line. Both, document (1) and the

patent application, refer to the HZ24 plasmid for transfecting DG44 CHO cells and carrying out dihydrofolate reductase/methotrexate (DHFR/MTX) gene amplification (cf. Example 7 on page 50 of document (1) and Example 1 on page 28 of the patent application). Both refer to the identification of ten clones which are characterised by identical designations (cf. page 51, left-hand column, Table in paragraph [0584] of document (1); page 29, Table 2 in paragraph [0187] of the patent application). After expanding six of these clones in culture and obtaining subclones by DHFR/MTX amplification, a subclone designated 3D3 5M (derived from clone 3D3) is used for the production of soluble rHuHP20 (cf. page 51, right-hand column, paragraphs [0585] and [0586] and Example 8 in document (1); page 29, paragraphs [0188] and [189] and page 30, Example 3 of the patent application).

14. According to Example 8 of document (1), the final productivity of the 3D3 5M clone (expanded in MTX and cultured for 14 days) was "1600 Units per ml with a maximal cell density of 6 million cells/ml" (cf. page 51, right-hand column, penultimate sentence in paragraph [0588] of document (1)). The harvest of the bioreactor at 14 days in Example 3.B of the patent application results in an identical value for the activity of soluble rHuHP20 but for "a maximal cell density of 8 million cells/ml" (cf. page 31, lines 30 to 32 of the patent application). In line therewith, 1676 units/mL are reported in the Table at the bottom of page 51 in document (1), and 991, 1319, 1670 and 1964 units/mL in Table 3 on page 31 of the patent application for the harvest titers of four batches derived from clone 3D3 5M. The activity of the soluble rHuHP20 measured in the clarified HCCF (separated by filtration from cells, cell debris and aggregates) of

these batches are 1039, 1425, 1768 and 2385 units/mL, respectively (cf. page 31, paragraph [0199] and first line of Table on page 32 of the patent application).

15. Although Example 9 of document (1) refers to the clarification of the conditioned media from clone 3D3, there is no value reported for the activity of the soluble rHuHP20. However, in view of the values disclosed in the patent application (*supra*), the board is convinced that the hyaluronidase activity of the soluble rHuHP20 comprised in these clarified conditioned media does not fall within the range defined in claim 1. Thus, there is no disclosure in document (1) of a clarified HCCF comprising soluble rHuPH20 with an enzymatic activity as defined in claim 1.

16. Example 9 in document (1) refers to the clarification of the conditioned media "by depth filtration and tangential flow diafiltration" (cf. page 52, left-hand column, paragraph [0590] of document (1)). Tangential flow filtration is also used in Example 3.B of the patent application for concentrating the clarified HCCF (cf. paragraph [0199] of the patent application) and the hyaluronidase activity reported for the four batches derived from clone 3D3 5M, once concentrated, are all greater than 5.000 units/mL. However, as stated above (cf. point 8 *supra*), concentrated HCCF is excluded from the scope of claim 1.

17. The board agrees with the appellant that a skilled person, using common general knowledge, would immediately recognise and easily distinguish clarified HCCF from concentrated clarified HCCF. The compositions of standard/commercial media suitable for culturing CHO cells - such as the chemically defined CD CHO and

CHO CDM media used in Example 3 of the patent application and Example 8 of document (1), respectively (cf. paragraph [0192] of the patent application; paragraph [0588] of document (1)) - are known in the art and available to the skilled person. The concentration of compounds (salts, buffers, inorganic compounds, trace elements, etc.) in clarified HCCF as harvested and separated from cells, cell debris and aggregates differs from that in clarified and concentrated HCCF. A skilled person is thus in a position to distinguish both products. Therefore, the board considers the concentrated HCCF cited in Example 9 of document (1) to fall outside the scope of claim 1.

18. In the decision under appeal, the examining division observed that there is no limitation as regards culture and harvest conditions in claim 1 and therefore considered the claimed HCCF to be characterised by "undefined impurities that are harvested along with the hyaluronidase". With reference to decision T 80/96 (OJ EPO 2000, 50), it stated that novelty could not be acknowledged on the basis of undefined impurities.

18.1 In point 4 of the Reasons for decision T 80/96, the board stated that claim 3 of the main request underlying that decision related to a product as such, namely a preparation containing L-carnitine-L-tartrate (active agent) in powder form with an undefined auxiliary substance. Claim 3 "includes every conceivable therapeutical and non-therapeutical use of the said preparation in powder form". The board observed that neither the structure nor the substantive function of the auxiliary substance was defined, and stated that "claim 3 ... does not give the person skilled in the art any specific guidance as to how the

claimed product should be formed ... Accordingly, an unlimited number of theoretically possible auxiliary substances with no details as to their structure and effect cannot be deemed in a claim to be a substantive addition to a structurally defined product. It does not therefore either change or add to the subject-matter defined in the claim, in other words the claimed product". Therefore, the board concluded that this "non-defined auxiliary substance of unspecified effect ... cannot be used under Article 54 EPC as a delimiting feature in the said product claim".

18.2 In the board's view, the present case is not comparable with that underlying decision T 80/96, because claim 1 of the main request provides detailed guidance as to how the claimed HCCF is obtained. Contrary to claim 3 of the request underlying decision T 80/96, claim 1 defines structural and functional features as well as features related to the method of production of the HCCF. Regardless of the particular conditions used for culturing and harvesting the cell culture fluid of claim 1, it must be derived from media suitable for culturing CHO cells and producing recombinant soluble rHuHP20 with enzymatic activity. As stated in point 17 *supra*, standard/commercial culture media for CHO cells are known in the art - as shown, for instance, by those exemplified both in the patent application and in document (1). Although there might be variation in the composition of these media, this variation does not result in an "unlimited number of theoretically possible ... substances with no details as to their structure and effect". Likewise, although the features related to the method of production in claim 1 may be broadly defined, they limit the scope of claim 1. In fact, by excluding concentrated HCCF, they delimit the

claimed HCCF from the HCCF disclosed in document (1) (cf. points 16 and 17 *supra*).

19. Thus, the main request fulfils the requirements of Article 54 EPC.

Article 56 EPC

20. The examining division identified document (1) as the closest prior art and, starting therefrom, formulated the objective technical problem as the provision of a HCCF comprising an increased concentration of hyaluronidase. The appellant does not contest the identification of document (1) as the closest prior art but formulates the technical problem as the provision of an improved starting material (clarified HCCF) for the purification of soluble rHuHP20.

21. In both, document (1) and the patent application, the clarified HCCF is used, after concentration and buffer exchange, for the purification of soluble HuPH20. There is no disclosure of any use or purpose for the clarified HCCF other than the purification of soluble HuHP20. In this sense, the claimed HCCF is seen as an intermediate product (cf. "Case Law", *supra*, I.D.9.8.4, 251) and the technical problem formulated by the appellant is appropriate.

22. The proposed solution to this problem is the HCCF of claim 1.

23. The results reported in the examples of the patent application, in particular in Examples 4 to 8 (cf. point 11 *supra*), show that the claimed subject-matter solves this technical problem.

24. The examining division, without citing any other document from the prior art, decided that the solution of the objective technical problem was obvious in the light of routine techniques available to the skilled person, and referred to three examples to support its decision, namely the addition of purified soluble HuHP20 to the HCCF described in document (1), the concentration of said HCCF, and the use of a stronger promoter in the constructs described in document (1). However, the board cannot agree with the examining division.

24.1 The board notes that, when considering the clarified HCCF as an intermediate product for use in the purification of soluble rHuHP20, the addition of (already) purified or pure rHuHP20 to the HCCF described in document (1) makes, although technically possible, no sense and is therefore not obvious.

24.2 Although the concentration of the HCCF described in document (1) is an obvious step in the purification of soluble rHuHP20, this step does not result in the claimed product (non-concentrated clarified HCCF) but in a different product (concentrated clarified HCCF) which, as stated in points 16 and 17 *supra*, differs in its composition and properties from the claimed product.

24.3 The expression vector used in Examples 7 and 8 of document (1) for transfecting the DG44 CHO host cells is described in Example 6 and comprises "a Cytomegalovirus immediate-early enhancer/promoter region (CMV)". Expression of this "construct ... results in a single mRNA species driven by the CMV promoter" (cf. page 50, right-hand column, last sentence of first paragraph). Reference is also made in

the description of document (1) to other promoters known in the art as well as to increasing the efficiency of expression by the inclusion of enhancers appropriate to the cell system in use (cf. pages 19 and 20, paragraphs [0236] to [0238]).

Although the CMV promoter is known in the art as variable, i.e. very strong in some cell types and rather weak in others, the board agrees with the appellant that this promoter is commonly used and recognized as a strong promoter for driving recombinant protein expression in CHO cells. It may be obvious for a skilled person to use other, alternative strong enhancer/promoters for expressing rHuHP20 in DG44 CHO host cells. The question is however, whether in doing so, it would have been reasonable to expect a significant increase (greater than 5000 units/mL) in the production of soluble rHuHP20. Indeed, a more than 3-fold higher activity is reported than that described in document (1) (1600 units/mL). In the present case, there is no evidence of any obvious alternative strong enhancer/promoters and their effects. In the absence thereof, such an increase in activity could not be reasonably expected.

25. Although the skilled person is defined in the case law as being cautious and having a conservative attitude (cf. "Case Law", *supra*, I.D.8.1.3, 205), it is also acknowledged that it is within the normal tasks of a skilled person to further develop the existing state of the art by routine adaptations and use of known alternatives (cf. T 688/14 of 24 July 2019, point 25.1 of the Reasons, and the case law cited therein). In the light thereof, the board agrees with the examining division that, starting from the closest prior art document (1), it would have been obvious for a skilled

person to look for possible alternatives, such as codon optimisation, optimisation of media components and culture conditions, etc., in order to improve the HCCF described in document (1). However, as for the replacement of the CMV promoter by other strong promoters, there is no evidence on file that a skilled person trying these alternatives and routine adaptations, would have had a reasonable expectation of successfully obtaining a HCCF with the activity of claim 1. Under these circumstances, the board considers that the claimed subject-matter could only be regarded as obvious with the benefit of hindsight.

26. In view of the documents and evidence on file, the main request is considered to fulfil the requirements of Article 56 EPC.

Conclusion

27. Since the main request fulfils the requirements of the EPC, there is no need for the board to examine any of the appellant's auxiliary requests.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance with the order to grant a patent with the following claims and a description to be adapted:

   Claims:
   Nos. 1 to 4 of the Main Request received during the oral proceedings of 24 January 2020.

The Registrar: The Chairman:

A. Chavinier-Tomsic B. Stolz

Decision electronically authenticated