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**Datasheet for the decision
of 28 May 2019**

Case Number: T 2091/13 - 3.3.08

Application Number: 01982192.5

Publication Number: 1334182

IPC: C12N9/50, C12N15/59, A23C19/032

Language of the proceedings: EN

Title of invention:
METHOD OF PRODUCING NON-BOVINE CHYMOSIN AND USE HEREOF

Patent Proprietor:
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Eidgenössische Technische Hochschule (ETH)

Opponent:
DSM IP Assets B.V.

Headword:
Camelidae chymosin/CHR HANSEN, ETH

Relevant legal provisions:
EPC Art. 54, 56, 83, 123(2), 123(3)

Keyword:
Main request - requirements of the EPC met (yes)

Decisions cited:

Catchword:



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Case Number: T 2091/13 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 28 May 2019

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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 25 July 2013
rejecting the opposition filed against European
patent No. 1334182 pursuant to Article 101(2)
EPC.**

Composition of the Board:

Chairman B. Stolz
Members: D. Pilat
 J. Geschwind

Summary of Facts and Submissions

- I. European patent No. 1 334 182 with the title "Method of producing non-bovine chymosin and use hereof" was granted on European patent application N°01982192.5 filed as an international application under the Patent Cooperation treaty as WO 2002/036752 (in the following "the patent application"). The patent was granted with 44 claims.
- II. An opposition was filed on the grounds set out in Articles 100(a) EPC in conjunction with Articles 54 and 56 EPC, 100(b) and (c) EPC. The opposition division decided, at the oral proceedings on 3 July 2013, that the patent met the requirements of the EPC and rejected the opposition.
- III. The opponent (appellant) lodged an appeal against this decision.
- IV. The patent proprietor (respondent) replied to appellant's statement of grounds of appeal and submitted eleven new auxiliary requests, in addition to the nine auxiliary requests submitted on 3 June 2013 in opposition proceedings.
- V. The board summoned the parties to oral proceedings and, in a communication sent in preparation of the oral proceedings, expressed its provisional opinion, inter alia on issues concerning Articles 123(2), 83, 54 and 56 EPC.
- VI. In reply to the board's communication, the respondent submitted a reduced set of new auxiliary requests 1 to 3, as well as documents D27 to D30.

- VII. Oral proceedings were held on 28 May 2019 in the presence of both parties.
- VIII. The respondent withdrew all previous auxiliary requests during oral proceedings and replaced them with new auxiliary requests 1 to 3 filed on 15 April 2019. At the very end of the oral proceedings, he made auxiliary request 1 its main request.
- IX. Claim 1 of the main request reads as follows:

"1. Use of a composition comprising a non-bovine pre-prochymosin, prochymosin or chymosin produced by a method comprising the steps of

(i) isolating or constructing a nucleic acid sequence coding for the pre-prochymosin, prochymosin or chymosin, wherein the coding sequence is derived from a mammalian species selected from the group consisting of a Camelidae species.

(ii) constructing an expression vector comprising said coding sequence and, operably linked thereto, appropriate expression signals permitting the pre-prochymosin, prochymosin or chymosin to be expressed in a host cell selected from a bacterial cell, fungal cell, yeast cell, or plant cell,

(iii) transforming said host cell with the expression vector,

(iv) cultivating the thus transformed host cell under conditions where the coding sequence is expressed, and

(v) harvesting the pre-prochymosin, prochymosin or chymosin,

in the manufacture of cheese from cow's milk."

Claim 3 concerns a method of manufacturing cheese, comprising adding a milk clotting effective amount of the composition comprising a non-bovine pre-prochymosin, prochymosin or chymosin to cow's milk and carrying out appropriate further cheese manufacturing steps, wherein the composition comprising a pre-prochymosin, prochymosin or chymosin is derived from a Camelidae species and is produced by a method comprising the steps identified in claim 1.

Claim 5 concerns a method of manufacturing cheese, comprising adding a milk clotting effective amount of a non-bovine prochymosin or chymosin to cow's milk and carrying out appropriate further cheese manufacturing steps, the non-bovine prochymosin or chymosin having in said milk a C/P ratio in the range of 2-20, wherein the non-bovine prochymosin or chymosin is recombinantly produced using a coding sequence derived from a mammalian species selected from the group consisting of a Camelidae species in a host selected from a bacterial cell, fungal cell, yeast cell, or plant cell.

Dependent claims 2, 4 and 6 define specific embodiments of claims 1, 3 and 5, respectively.

X. The following documents are referred to in this decision:

D3: J. Wangoh et al., *Milchwissenschaft* (1993), Vol. 48(6), pages 322-325;

- D6: S. Kappeler, Dissertation ETH No. 12947, Swiss Federal Institute of Technology, Zurich (1998);
- D7: GenBank Accession Number: AJ131677.1
(<http://www.ncbi.nlm.nih.gov/nucore/11990125>);
- D9: M.A. El-Batawy, Egyptian J. Dairy Sci. (1991), Vol. 19, pages 315-325;
- D10: M.A. El-Batawy, Egyptian J. Dairy Sci. (1992), Vol. 20, pages 329-339;
- D12: M.A. El-Batawy, Egyptian J. Dairy Sci. (1991), Vol. 19, pages 117-130;
- D27: Encyclopedia of Food Microbiology, Academic Press 2000, pages 372-392, Chapter "Cheese".
- D29: Methods in Molecular Biology, Recombinant Gene Expression: Reviews and Protocols, Second Edition, Chapter "Production of Recombinant Proteins", (2004) Vol. 267, pages 15 to 51.

XI. The submissions made by the appellant insofar as relevant to the present decision, may be summarized as follows:

Article 123(2), (3) EPC

Claim 1 was directed at the use of a composition comprising a camel pre-prochymosin, prochymosin or chymosin. Claim 1 was neither restricted to the use of an effective amount of a milk clotting composition nor did it require further appropriate cheese manufacturing steps to be carried out. There was no basis on page 4, lines 16 to 18 of the patent application for a

composition having a high clotting activity on cow's milk, and for a method of manufacturing cheese, wherein both the steps of adding an effective amount of a milk clotting composition to milk and of carrying out appropriate further cheese manufacturing steps were missing (see page 15, lines 1-7, and page 16, lines 13-16, of the patent application). As a result, claim 1 covered the use of a composition for a single step cheese manufacturing process which was nowhere disclosed in the patent application (see also document D27 page 372, col.2 second bullet point). Besides, claim 1 did not specify a higher yield of cheese when a recombinant pre-prochymosin, prochymosin or chymosin from camelidae species was used (see page 15, lines 19-20 of the patent application). Thus, claim 1 encompassed subject-matter beyond the content of the patent application.

Claim 1 was derived from granted claim 34 referring back to claim 31, which required both the composition as defined in granted claim 31 to be used and appropriate further cheese manufacturing steps to be carried out. Since the appropriate further cheese manufacturing steps were absent from claim 1, the scope of protection was broader than that of granted claim 34. This contravened Article 123(3) EPC.

Article 83 EPC

In paragraph 2.14.5 of the decision under appeal, doubts were raised by the opposition division whether a camel chymosin could be expressed in camel cells. During examination of the divisional application EP10185159.0 / EP2365069 of the present parent application a lack of sufficiency objection was raised insofar as the claims encompassed the use of camel

chymosin sequences other than that incorporated into the deposited strain CBS108914. Thus, there were serious doubts that the invention could not be carried out over the entire scope of claim 1. The requirements of Article 83 EPC were therefore not met.

Article 54(1)(2) EPC

All the claims lacked novelty over document D10, which disclosed that Ras cheese produced by a mixture of adult camel rennet (ACR) and calve's rennet (CR) yielded the highest score. The use of this mixture as a substitute for CR in manufacturing Ras cheese was recommended (see D10 abstract, last two sentences). The enzyme in adult camel rennet (ACR) and in the composition according to claim 1 were indistinguishable. The same conclusion applied to claim 2. The effect explicitly mentioned in claim 4 was obtained inevitably when the method of claim 3 was carried out. Document D10, Table 1 showed that the yield of Ras cheese during ripening was always higher when the cheese was made with adult camel rennet alone (C) compared to cheese made with calves rennet (A). Thus, there was no difference between the method of claim 4 and the one disclosed in document D10. Finally, the specific milk clotting activity (C) over the (non-specific) proteolytic activity (P-value), presented as a C/P ratio in claim 5, was asserted to be intrinsic to the camelidae chymosin comprised in the composition used in the method of claim 4. Thus, claim 5 was deprived of novelty by the method disclosed in document D10.

Article 56 EPC

Document D10 was the closest prior art. It described the use of adult camel rennet (ACR) alone or mixed with calves rennet (CR) in making Ras cheese and provided evidence for an increased yield (see abstract; Table 1 (C)). The method of producing cheese disclosed in document D10 differed from the use of claim 1 in that it used a composition comprising a recombinantly produced pre-prochymosin, prochymosin or chymosin from Camelidae species. No technical effect could be derived from said difference. Thus, starting from the closest prior art, the technical problem to be solved was the provision of an alternative method to the one disclosed in document D10. The solution was the use of a recombinant pre-prochymosin, prochymosin or chymosin from Camelidae species. Thus, faced with the technical problem of providing an alternative method to the one disclosed in document D10, and to avoid expensive camel calf slaughter, the skilled person would have been motivated to use a recombinant pre-prochymosin, prochymosin or chymosin in the manufacture of cheese. A camel chymosin cDNA sequence was disclosed both in documents D7 and D6 (see Fig.4.11). Document D6 mentioned further that the "use of camel chymosin may help to prevent the formation of bitter peptides [...], and therefore help to promote consumer acceptability of cheese products in camel keeping countries." (see bridging paragraph on page 58 to 59 of document D6) and that "[L]arge-scale production of this enzyme, e.g. by recombinant methods, should be envisaged therefore". Thus, faced with the technical problem of providing an alternative method to the one disclosed in document D10, i.e. keeping an increased cheese yield, the skilled person would have turned to a method of producing cheese using recombinant camel chymosin, as suggested on page 59 of document D6, with the concomitant prospect of reducing bitter peptides - even

though this beneficial effect was not a functional requirement of claim 1 - and would have tested it on cow's milk. Hence, the requirement of Article 56 EPC was not met.

XII. The submissions made by the respondent concerning issues relevant to this decision, were essentially as follows:

Article 123(2), (3) EPC

The method of claim 3, using a composition comprising a pre-prochymosin, prochymosin or chymosin from Camelidae species, was derived from original claims 38, 35 and 1. Its reference to cow's milk and host cells were derived from the patent application on page 4, lines 16 to 18, page 15, lines 1 to 7, lines 19 to 22 and line 31, page 16, line 13 and page 10, lines 6 to 9, respectively.

The use of the composition in the manufacture of cheese from cow's milk of claim 1 was derived from the patent application (page 4, lines 16 to 18, page 15, lines 1 to 7, lines 19 to 22 and line 31, page 16 line 13). The composition was derived from original claim 35 and the method steps incorporated therein were derived from its back reference to original claim 1. The host cells were disclosed on page 10, lines 6 to 9.

The patent application disclosed that camel enzyme had a high clotting activity on cow's milk (see page 4, lines 16 to 18 of the patent application). This implied that also a camel enzyme composition had this property. Moreover, the use of claim 1 was for the manufacture of cheese. There was thus no need to explicitly specify in claim 1 that an effective amount of a milk clotting composition was used or that cheese manufacturing steps

had to be carried out. Since the use of a composition as defined in claim 1 inevitably resulted in a higher yield of cheese, there was no need to introduce this effect into claim 1 either.

Granted claim 31 related to a composition comprising a non-bovine pre-prochymosin, prochymosin or chymosin produced by the method of any of claims 1 to 14. This claim covered therefore methods and uses of said composition. Hence, a method of manufacturing cheese using the composition of granted claim 31, as now claimed in claim 1, did not extend the scope of protection over that of the patent as granted.

Article 54(1)(2) EPC

ACR was shown to be a mixture of two milk clotting enzymes: pepsin and chymosin. Chymosin was present in a relatively small proportion (around 5 %, in contrast to 95 % pepsin (see Summary of D9)). A camel chymosin produced in a heterologous host cell, as defined in claim 1, was chemically different from the native chymosin comprised in the ACR, because "glycosylation profiles are protein-, tissue- and animal-specific" (see page 24 of document D29). It was also known that the milk clotting activity of aspartic acid proteases was dependent on their glycosylation state (see [0048] of the patent). Thus, in the absence of any evidence that the ACR composition disclosed in document D10 comprised chymosin which was indistinguishable from the chymosin obtained by the process defined in claim 1 and that the resulting C/P ratio of 2 to 20 was inevitably obtained, as required by claim 5, the claims were novel.

Article 56 EPC

Document D10 was never before considered to represent the closest prior art. Its use as closest prior art document created a fresh case.

Document D10 did neither disclose nor suggest the use of a composition comprising a recombinant camel chymosin for clotting cow's milk.

Document D3 reported that camel rennet and calf rennet extracts, when compared, showed equal activity to coagulate camel and cow milk (see abstract, last sentence; p.323, col.1 bridging paragraph; Fig.4, fraction 1; Document D6 page 49, lines 17-18). Although the maximum clotting activity of the first fraction from calf rennet extract did not coincide with the maximum absorbance at 226 nm, e.g. with the highest protein concentration, the two peaks of the first fraction of the camel rennet extract coincided well with the absorbance peak at 226 nm. Although, the first fraction of calf rennet contained chymosin and the second fraction pepsin (see document D3 page 323 col.2, lines 3-6), there was no direct and unambiguous disclosure that the first fraction of camel rennet extract contained chymosin and the second fraction pepsin.

It was shown in the patent application that the recombinant chymosin of *Camelus dromedarius* had an average clotting activity per mole (C-value) of 180% compared to that of the bovine chymosin (see Table 5.1) and a lower non-specific proteolytic activity (P) compared to the bovine chymosin (see example 4). The technical problem was therefore the provision of a composition with high milk clotting activity and high

specificity, which was represented by a higher C/P ratio.

Document D6 speculated that camel chymosin was better suited for rennet coagulation of camel milk than calf chymosin. However, there was no indication in this document that the use of camel chymosin led to an improved yield of cheese, a higher specific milk clotting activity, represented by a higher C/P value, and prevented the formation of bitter peptides during cheese ripening, when cow milk was used. On the contrary, document D6 considered on page 48, last paragraph, citing document D3, that on camel milk "... the main clotting activity of calf rennet resided in the pepsin fraction, whereas the main clotting activity of camel rennet originated from the chymosin fraction." This showed that the effect reported in document D10 was due to pepsin.

Document D9 disclosed that adult camel rennet was a mixture of two clotting enzymes comprising around 5 % chymosin and 95 % pepsin (see Summary). Since, the composition comprised a large proportion of pepsin, known to have a broader specificity, the formation of bitter peptides was not expected to be reduced to the same extent as when a high proportion of camel chymosin was present in the composition.

As a consequence, the technical problem underlying the invention was to provide a composition capable of preserving good cheese yield, as disclosed in D10, reducing bitter peptide formation and including other advantages, e.g. to use a purified and lower amount of enzyme. Thus, the technical problem had to be considered as the provision of an improved composition

for manufacturing cheese from cow's milk. The problem was shown to be solved in example 1 of the application.

In the light of the prior art, there was no reasonable expectation of success of finding these advantages in document D6.

XIII. The appellant requested that the decision under appeal be set aside and the patent be revoked.

XIV. The patent proprietor (respondent) requested that the decision under appeal be set aside and the patent be maintained on the basis of the main request filed at the oral proceedings before the board.

Reasons for the Decision

Main Request

The main request corresponds to auxiliary request 16, originally submitted as auxiliary request 9 in opposition proceedings. In response to issues raised in the board's communication, claim 1 was amended to read "use of a composition ... in the manufacture of cheese from cow's milk" and claim 3 was deleted. The appellant had no objections to its admission.

Article 123(2) EPC

1. The appellant asserted that claim 1 contravened Article 123(2) EPC for two reasons. First, because it referred to the use of a composition comprising a Camelidae enzyme, while the patent application disclosed only the use of a camel enzyme having high clotting activity. Second, claim 1 neither required the achievement of a higher yield nor the use of an effective amount of a

milk clotting composition and did not specify further appropriate steps for manufacturing cheese. Hence, claim 1 also covered the use of a composition for the manufacture of cheese with a single step process for which no basis could be found in the patent application.

2. The board agrees with the respondent that the method of claim 3, using a composition comprising a pre-prochymosin, prochymosin or chymosin from Camelidae species, can be derived from original claims 38, 35 and 1.

3. Original claim 38 relates to a method of manufacturing cheese and refers back to any one of claims 35 to 37. Original claim 37 identifies four different origins of chymosin, whereas claim 35 characterizes the enzyme of the composition by means of a process as defined in claims 1 to 16. Thus, claim 38 referring back to claims 37 and 35 characterizes a composition comprising a pre-prochymosin, prochymosin or chymosin producible by any one of the methods of claims 1 to 16, which originates from one of the four options, i.e. Camelidae species, listed in claim 37. The use of enzymes with this preferred origin is also disclosed in Examples 3 to 6, 8 of the patent application. The use of plant cells, bacterial, fungal or yeast cells, is directly and unambiguously derivable from page 10, lines 6 to 9, referring to various host organisms "in accordance with the invention", and claim 10.

The use of cow's milk in the manufacture of cheese is explicitly disclosed on page 4, lines 16 to 18, and on page 15, line 31. The cow's milk is furthermore one of several milk types proposed on page 15, lines 1 to 7, and is explicitly used for assessing the camel

chymosin's effect in examples 7 and 9. The use of cow's milk in the manufacture of cheese is therefore directly and unambiguously derivable from the patent application.

Thus, the method of claim 3 meets the requirements of Article 123(2) EPC.

4. Since there is a direct and unambiguous disclosure of the method of claim 3, comprising the addition, i.e. the use, of a milk clotting effective amount of a composition comprising prepro-chymosin, prochymosin or chymosin to cow's milk, the use of the same composition for the same purpose according to claim 1 is also directly and unambiguously disclosed.
5. Since the purpose of claim 1 is the use of the composition for manufacturing cheese, the use of an effective amount of a milk clotting composition to form the curd is an implicit feature of claim 1 as are appropriate further cheese manufacturing steps. The higher yield of cheese is the result of the claimed method and use and needs no mention in the claims (see examples and page 15, lines 19-22 of the patent application).
6. Appellant argued, by reference to document D27, col.2, last bullet point, that claim 1 also contravened Article 123(2) EPC because it encompassed the use of the composition for the manufacture of cheese in a one step process.

The board cannot follow this argument because, as stated above, the use of an effective amount of the composition and further appropriate cheese manufacturing steps are implicit features of claim 1.

Moreover, these additional steps are unspecifically defined in the patent application, thus embracing steps of any type, also steps of a single step manufacturing process, which does not consist of literally only one single step.

7. The board concludes that claim 1 does not contravene Article 123(2) EPC.

Article 123(3) EPC

8. The appellant argued that claim 1 contravened Article 123(3) EPC because it derived from granted claim 34 which included the carrying out of further appropriate cheese manufacturing steps. Since further appropriate cheese manufacturing steps were not mentioned in claim 1, its scope of protection extended beyond the scope of protection of the claim as granted.
9. As explained above, the allegedly missing features are intrinsic features of claim 1. Moreover, claim 31 as granted was directed at a composition comprising a non-bovine pre-prochymosin, prochymosin and chymosin produced by a method according to granted claims 1 to 14. The scope of protection of granted claim 31 extends therefore to any use of said composition in whichever method of manufacture, including the use of claim 1. Thus, claim 1 does not offend Article 123(3) EPC.

Article 83 EPC

10. Based on a statement by the opposition division in paragraph 2.14.5 of the decision under appeal which related to novelty of the claimed subject matter, the appellant concluded that the opposition division itself, despite its conclusion to the contrary when

discussing sufficiency of disclosure, had doubts whether the enzyme could be expressed in camel cells. The appellant argued furthermore that objections of lack of sufficiency of disclosure were also raised during the examination of a divisional application of the present patent application. These objections were not substantiated any further.

11. The board notes that the appellant did not provide any evidence to support its allegations. There are thus no verifiable facts on file that would allow the board to examine the substance of this objection. Hence, the board considers the requirements of Article 83 to be met.

Article 54 EPC

12. Claim 1 is directed at the use of a composition comprising pre-prochymosin, prochymosin or chymosin from a Camelidae species produced by a method comprising steps (i) to (v) in the manufacture of cheese from cow's milk (see item X, above).
13. The appellant submitted that the use of claim 1 was anticipated by the disclosure of document D10.
 - 13.1 Document D10 discloses Ras cheese produced by adult camel rennet (ACR) and calves rennet (CR) separately and in a mixture (1:1). Ras cheese is made from cow's milk (page 330, first paragraph). The mixture (1:1) of rennets obtained the highest score and was recommended as substitute for CR in manufacturing Ras cheese (see D10 abstract, last two sentences). The effect of mixing CR with ACR on the yield of Ras cheese during ripening was always a higher yield when compared to cheese made with calves rennet (see Table 1 of document D10).

13.2 Claim 1 is limited to the use of chymosin from a camelidae species obtainable by expression of the respective gene in bacterial, fungal, yeast or plant cells but not mammalian cells. It is generally known that "glycosylation profiles are protein-, tissue- and animal-specific" (see document D29 page 24). It is also known that the milk clotting activity of aspartic acid proteases, including chymosin, is dependent on their glycosylation state (see patent [0048]). Thus, the pre-prochymosin, prochymosin or chymosin of a camelidae species expressed in a bacterial, fungal, yeast or plant cell, differs in its chemical composition from chymosin expressed in camel cells, as is the case for the chymosin present in the camel rennet described in document D10.

In the absence of any evidence to the contrary, the board can only conclude that the use of camel rennet, comprising a chemically distinct chymosin, for the manufacture of Ras cheese is not encompassed by the scope of claim 1. Thus, the the subject-matter of claim 1 is novel.

13.3 The conclusion drawn for claim 1 applies mutatis mutandis to the method of claims 3 and 5, which both include the use of a composition comprising a recombinant camel chymosin, incorporating all the technical features conferred by the method of production defined in claim 1, for the manufacture of cheese from cow's milk. Hence, for the same reason as for claim 1, the subject-matter of claims 3 and 5 is novel.

Article 56 EPC

14. The appellant considered document D10 to represent the closest prior art for the subject-matter of all the claims.
15. The respondent considered the disclosure of documents D3, D6, D9 and D10 to be relevant for the assessment of inventive step.
16. The respondent submitted that document D10 had not been used as closest prior art document until this point in time. In doing so, the appellant therefore presented a fresh case which, under Article 13 RPBA, should not be admitted.
17. Document D10 was filed with the statement of grounds of opposition and cited in support of novelty and inventive step attacks against granted claims 43 and 44 relating to the manufacture of cheese from milk and cow milk in particular (see pages 19, 20, 37 and 38). The document was again cited in the statement of grounds of appeal for an inventive step attack on claim 43.

Thus, the respondent must be familiar with the contents of this document. Further, respondent's limitation of the claims to the use of an enzyme, obtainable by recombinantly producing it in bacterial, fungal, yeast or plant cells, for the manufacture of cheese from cow's milk, created a new case which justifies a re-assessment of the documents suggested to represent the closest prior art.

18. The closest prior art is generally a document disclosing subject-matter conceived for the same purpose or aiming at the same objective as the claimed

invention and having the most technical features in common with said invention requiring a minimum of structural modifications (see Case Law of the Boards of Appeal, I.D.3.1).

19. Document D3 is a scientific publication that "... aims at extracting camel rennet and testing its ability to coagulate camel and cow milk compared to calf rennet extract, chymosin and pepsin" (see abstract). However, this document does not mention the manufacture of cheese, let alone the manufacture of cheese from cow's milk with camel rennet.
20. Document D6 is a PhD thesis directed at the analysis of the composition and structure of camel milk proteins. It describes renneting enzymes and functional aspects related to said camel rennet. The use of the camel chymosin is indicated to maybe help to prevent the formation of bitter peptides during cheese ripening, which impair the taste, and therefore help to promote consumer acceptability of cheese products in camel keeping countries. The large scale production of recombinant camel chymosin is proposed.
21. Document D9 discloses the fractionation of adult camel rennet (ACR) and the characterization of its enzymatic composition.
22. Document D12 is a scientific publication which analyses the effect of some factors on the milk clotting activity of adult camel rennet extract (ACR) in comparison to a calves rennet extract (CR).
23. Documents D6, D9 and D12 do not mention the use of camel rennet or chymosin in the manufacture of cheese from cow's milk, be it explicitly or implicitly.

24. Document D10 is the only one whose purpose, i.e. the use of camel rennet for the manufacture of Ras cheese from cow's milk, corresponds to the purpose of claim 1. Thus, document D10 represents the closest prior art.
25. The appellant submitted that the subject matter of claim 1 differed from the method of producing cheese described in document D10 only in that a composition comprising a recombinant pre-prochymosin, prochymosin or chymosin from a Camelidae species was used.
26. The appellant asserted that no technical effect could be derived from this difference.
27. The patent application shows that the recombinant chymosin of *Camelus dromedarius*, obtained from fungal cells, has an average clotting activity per mole (C-value) of 180% compared to the bovine chymosin (see Table 5.1) and has a lower non-specific proteolytic activity (P) compared to the bovine chymosin (see example 4). The patent discloses further that the use of a recombinant camel chymosin in cow's milk resulted in a shorter coagulation time (12.20 min. vs. 12.66 min) and higher curd strength (50.56 vs. 18.24) compared to camel raw milk (see example 7, Table 7.1).
28. In view of the technical effects resulting from the differences between the subject-matter claimed and the closest prior art, the objective technical problem can be defined as the provision of an improved composition for manufacturing cheese from cow's milk, while preserving good yield of cheese.
29. The appellant submitted that the underlying technical problem was not plausibly solved when using recombinant

chymosin from any camelidae species other than C. dromedarius because the patent provided no evidence to this effect.

30. However, in the absence of evidence substantiating appellant's argument, the use of chymosin from C. dromedarius, as exemplified in the patent, is sufficient to render a beneficiary effect plausible when using chymosin from other camelidae species.

Therefore, and in view of the experimental data provided in examples 4 and 7 of the patent, the board is satisfied that the subject-matter of claim 1 indeed provides a solution to this technical problem.

31. The appellant held that starting from document D10, the skilled person, faced with the technical problem identified above, would have been motivated to replace the camel rennet extract by its recombinant form with the concomitant prospect of achieving a reduction of bitter peptides (see document D6).

32. The board is not convinced by this argument. Firstly, document D10 recommends the use of a 1:1 mixture of camel and calf rennets and does not motivate the skilled person to use recombinant camel chymosin. Secondly, there is no indication in document D10 that the activity in the camel rennet extract, made up of approximately 95% pepsin and around 5% chymosin (see document D9), responsible for the cow milk's clotting, must be assigned to the chymosin fraction. Thirdly, even if it is assumed that the chymosin fraction of the camel rennet is responsible for the increased yield of Ras cheese, there is no indication in the prior art that a recombinant camel chymosin, expressed in heterologous host cells such as bacterial, fungal,

yeast or plant cells, will keep a milk clotting activity resulting in an increased yield of Ras cheese. On the contrary, the milk clotting activity of aspartic acid proteases, which includes chymosin, was known to be dependent on their glycosylation profile (see patent [0048]). Thus, even if document D10 discloses the use of an adult camel rennet (ACR) for producing Ras cheese leading to an increase in yield, moisture, titratable acidity, total volatile fatty acids and soluble nitrogen, the skilled person would not have derived from said document any indication how to improve the manufacture of cheese from cow's milk or an incentive to turn to document D6.

33. Although document D6 suggests the use of recombinant camel chymosin for the production of cheese to promote consumer acceptability of cheese products in camel keeping countries, there is no pointer in said document which would motivate the skilled person to use a camel enzyme in the manufacture of cheese from cow's milk, let alone to use a recombinant camel chymosin, expressed in either bacterial, fungal, yeast or plant cells, in order to improve the manufacture of cheese from cow's milk. Even if document D6 states that the use of a camel enzyme may help to prevent the formation of bitter peptides during cheese ripening, this statement refers undoubtedly to cheese obtained from camel milk. The skilled person cannot extrapolate from this statement that the prevention of the formation of bitter peptides during cheese ripening from cow's milk would occur too.

34. A replacement of an adult camel rennet extract by a composition comprising a recombinant camel chymosin, expressed in bacterial, fungal, yeast or plant cells for manufacturing cheese from cow's milk could have

been envisaged, but since the milk clotting activity of aspartic acid enzymes, which includes chymosin, was known to be dependent on their glycosylation profile and no factor is identifiable in document D10 pointing towards how to improve the manufacturing of cheese from cow's milk, the skilled person would not have done so. And even if, for the sake of the argument, the skilled person would have done so, it had no reasonable expectation of solving the technical problem posed. The skilled person would have rather been deterred from using recombinantly produced chymosin, since the effect of expressing camel chymosin in a heterologous system on the glycosylation profile and hence, the effect on the chymosin's enzymatic activity and accordingly even further on the manufacturing of cheese from cow's milk was unpredictable. Thus, the skilled person would not have arrived at the subject matter of claim 1 on the basis of documents D10 and D6 in an obvious way.

Nor would he, for the same reasons, have arrived at the subject matter of claim 1 on the basis of document D10 in combination with any of the other documents on file.

- 34.1 Thus, the subject matter of claim 1 involves an inventive step.
- 34.2 For the same reasons, claims 3 and 5, incorporating the use of claim 1 in methods of manufacturing cheese from cow's milk, involve an inventive step.
- 34.3 Consequently the main request meets the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the opposition division with the order to maintain the patent on the basis of claims 1 to 6 of the main request filed during oral proceedings on 28 May 2019 and a description to be adapted.

The Registrar:

The Chairman:



L. Malécot-Grob

B. Stolz

Decision electronically authenticated