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D E C I S I O N
of 11 February 2000

Case Number: T 0972/94 - 3.3.4

Application Number: 87110307.3

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Title of invention:

A process for producing bovine lactoferrin in high purity

Patentee:

Morinaga Milk Industry Co., Ltd.

Opponents:

01: Société de Produits Nestlé S.A.

02: Kraye, Warner Dirk

Headword:

Lactoferrin/MORINAGA

Relevant legal provisions:

EPC Art. 54, 84, 123

Keyword:

"Clarity - yes"

"Added subject-matter - no"

"Novelty - yes"

Decisions cited:

Catchword:

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Boards of Appeal

Chambres de recours

Case Number: T 0972/94 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 11 February 2000

Appellant: Morinaga Milk Industry Co., Ltd.
(Proprietor of the patent) 33-1, Shiba 5-chome
Minato-ku
Tokyo-to 108-0014 (JP)

Representative: Ebner von Eichenbach, J.
Langner Parry
52-54 High Holborn
London WC1V 6RR (GB)

Respondent I: Société des Produits Nestlé S.A.
(Opponent 01) 55, Avenue Nestlé
CH-1800 Vevey (CH)

Respondent II: Krayner, Warner Dirk
(Opponent 02) c/o Koninklijke Nederlandse Zuivelbond FNZ
Volmerlaan 7
2280 HV Rijswijk (ZH) (NL)

Representative: Hatzmann, M.
Vereenigde Octrooibureaux
Nieuwe Parklaan 97
2587 BN 's-Gravenhage (NL)

Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 13 October 1994
revoking European patent No. 0 253 395 pursuant
to Article 102(1) EPC.

Composition of the Board:

Chairman: L. Galligani
Members: D. D. Harkness
C. Holtz

Summary of Facts and Submissions

I. This appeal concerns the issues of clarity required by Article 84 EPC, conformity with Article 123 EPC of the amended claims now on file as well as novelty of the subject-matter of these claims as required by Article 54 EPC.

II. The appellant (patent proprietor) requested that the decision of revocation of the patent by the opposition division be set aside and that the subject-matter of either the main or auxiliary request filed on 9 February 2000 be considered novel, and that the case be remitted to the first instance for prosecution of the issue of inventive step.

The respondents (opponents) requested that the appeal be dismissed on the ground that the claims of the requests on file were unclear and did not meet the requirements of Article 123(2) EPC.

III. Claims 1 and 3 of the main request read as follows:

"1. A process for producing bovine lactoferrin in high purity from raw milk materials containing skim milk or whey originating from cow's milk which process consists of:

(a) an adsorption step wherein said raw materials are contacted at a temperature between 0-60°C with a weakly acidic cation-exchanger which includes carboxymethyl groups as ion exchanging groups and which has an haemoglobin adsorbing property of more than 3.5g/100 ml of the Na form of the

swelled cationic-exchanger at 25°C,

- (b) a rinsing step wherein said exchanger is washed with rinsing means, said rinsing means consisting of water to remove substances other than those adsorbed to said exchanger, and
- (c) optionally a washing step wherein said exchanger is washed with further washing means, said further washing means being a relatively weak salt solution within a concentration range of 0.4-2.5 wt.% consisting of one or more of salts selected from the group consisting of sodium chloride, potassium chloride, calcium chloride and magnesium chloride to remove contaminants, and
- (d) a desorption step wherein the substances adsorbed to said exchanger are desorbed therefrom with desorbing means, said desorbing means being a salt solution consisting of one or more salts selected from the group consisting of sodium chloride, potassium chloride, calcium chloride and magnesium chloride to thereby yield highly purified bovine lactoferrin, wherein the purity of the yielded bovine lactoferrin ie. proportion (%) of lactoferrin to total proteins in the final product is equal to or more than 80% of the total proteins desorbed from said exchanger, wherein when said optional washing step is undertaken, said desorbing means is a relatively strong salt solution within a concentration range of 1.5-12 wt% consisting of one or more salts selected from said group of salts."

"3. A process for producing bovine lactoferrin in high purity from raw milk materials containing skim milk or whey originating from cow's milk which process consists of:

- (a) an adsorption step wherein said raw materials are contacted at a temperature between 0-60°C with a weakly acidic cation-exchanger which includes carboxymethyl groups as ion exchanging groups and which has an haemoglobin adsorbing property of more than 3.5 g/100 ml of the Na form of the swelled cationic-exchanger at 25°C,
- (b) a rinsing step wherein said exchanger is washed with rinsing means, said rinsing means consisting of water to remove substances other than those adsorbed to said exchanger, and
- (c) a washing step wherein said exchanger is washed with further washing means, said further washing means being a relatively weak salt solution within a concentration range of 0.4-2.5 wt.% consisting of one or more salts selected from the group consisting of sodium chloride, potassium chloride, calcium chloride and magnesium chloride to remove contaminants, and
- (d) a desorption step wherein the substances adsorbed to said exchanger are desorbed therefrom with desorbing means, said desorbing means being a relatively strong salt solution prepared within a concentration range of 1.5-12 wt% consisting of one or more salts selected from those described in step (c) above, wherein the said purity of the

yielded lactoferrin ie. proportion (%) of lactoferrin to total proteins in the final product is equal to or more than 95% of the total proteins desorbed from said exchanger."

IV. The following documents are relevant for the decision:

- D1: B. A. Law and B. Reiter, "The isolation and bacteriostatic properties of lactoferrin from bovine milk whey". Journal of Dairy Research (1977), vol. 44, 595-599.
- D2: T. Zagulski, Z. Jarzabek, A. Zagulska and J. Jedra, "A simple method of obtaining large quantities of bovine lactoferrin", Prace i Materialy Zootechniczne (1979), vol. 20, 87-101.
- D3: C. B. Laurell, "Quantitative estimation of proteins by electrophoresis in agarose gel containing antibodies", Analytical Biochemistry (1966), vol. 15, 45-52.

V. Claim 1 **as originally filed** in the European patent application read as follows:

"1. A process for producing bovine lactoferrin in high purity from raw milk-materials containing skim milk or whey originated from cow's milk which comprises:

- (a) adsorption step wherein said raw materials are contacted, at a temperature between 0-60°C, with weakly acidic cation-exchanger which includes carboxymethyl groups as ion exchanging groups and has haemoglobin adsorbing property more than

3.5 g/100 ml;

- (b) rinsing step wherein said exchanger is washed with water to remove substances other than those adsorbed to said exchanger; and
- (c) desorption step wherein the substances adsorbed to said exchanger are desorbed therefrom with a solution of one or more of salts to thereby yield highly purified bovine lactoferrin."

Claim 1 **as granted** had the following form:

"1. A process for producing bovine lactoferrin in high purity from raw milk materials containing skim milk or whey originated from cow's milk which comprises:

- (a) adsorption step wherein said raw materials are contacted, at a temperature between 0-60°C, with weakly acidic cation-exchanger which includes carboxymethyl groups as ion exchanging groups and has haemoglobin adsorbing property more than 3.5 g/100 ml of the Na form of swelled cation-exchanger at 25°C;
- (b) rinsing step wherein said exchanger is washed with water to remove substances other than those adsorbed to said exchanger; and
- (c) desorption step wherein the substances adsorbed to said exchanger are described [*desorbed*] therefrom with a solution of one or more of salts to thereby yield highly purified bovine lactoferrin."

Reasons for the Decision

1. The appeal is admissible.
2. Respondent II (Opponent 02) objected to the late filing of the claim requests on file and argued that they should not be admitted.

In the board's judgment, the new requests did not require the parties to spend an undue amount of time in order to understand the relevance of the amendments made. Said amendments were easily understood, they restricted the subject-matter claimed and rendered the requests more clear. Accordingly they are admitted.

Main request

3. *Clarity, Article 84 EPC*
 - 3.1 Respondent I (Opponent 01) argued essentially that claim 1 of this request did not satisfy the clarity requirements for the following reasons:
 - (a) The constitution of the water employed for the washing step was not defined, ie, there was no indication of which ions were present and whether or not it was ionised water.
 - (b) There was an overlap between the concentration ranges of the two salt solutions employed in the case that the optional washing step was carried out and this lead to confusion in respect of the necessary salt concentration for each of the

optional washing and lactoferrin desorption process steps.

- (c) The Laurell method for determination of lactoferrin purity is not the best method and leads to false results. It was not correct to calculate the percentage proportions of lactoferrin to the total proteins present based on an absorbancy of pure lactoferrin of 12,7 at 280 nm for a 1% solution. The Kjeldahl method was more reliable as a measure of proteins present.

3.2 Respondent II argued that the claims were not clear because:

- (i) The claims should be interpreted having regard to the disclosure of the specification as a whole, thus they included the use of buffer solutions as exemplified in Example 3 of the description in which a buffered potassium chloride solution containing citric acid was specified.
- (ii) The term "rinsing" was not clear as it could include rinsing with liquids other than water or water alone.
- (iii) It was not clear on what basis the purity of the product lactoferrin was measured because some protein was removed in the optional washing step whilst the remainder was eluted in the final desorption stage. The percentage yield may therefore be based on the sum of the two amounts of protein removed or alternatively only on that

obtained from the last process step. Further the wording on pages 5 and 6 of the description relating to the calculation of purity values was not clear and only imprecise values were obtained.

- 3.3 The appellant maintained that the claims were clear because the process "consisted" of three obligatory steps, adsorption, rinsing and desorption, and one optional washing step. No other process steps were involved.

The term "rinsing" was defined in the description at page 3, line 18 as being a water washing process, thus wherever "rinsing" was referred to this meant washing with water. Further it was not required that ionised water be used for washing, this was not essential for the process which washed the proteins as conventionally done in the prior art.

The desorption step and optional washing step were limited to employing only salt solutions consisting of one or more salts selected from sodium, potassium, calcium and magnesium chlorides, thus only these salts are present and buffers which required a weak acid and a salt of such an acid were excluded from the process.

There was no ambiguity in the claim deriving from the two overlapping concentration ranges of the salt solutions because it was specifically indicated that for the optional washing step use of a salt solution of lower concentration than that required by the desorption step was an obligatory feature of the process.

The appellant did not agree that the way in which purity had been calculated was inappropriate or incorrect. The method according to Laurell was well known in the art and was described in D3. It was immaterial which method was invoked. Each of the examples contained a calculation in respect of the purity of the final product and it was clear at page 5, line 54 of the patent in suit and in the Examples 2 and 8 that the purity calculation was only concerned with the desorption liquors, ie., recovered solution, from the last stage of the process.

- 3.4 The board agrees with the arguments presented by the appellant for the following reasons:

A claim which employs the "consisting" terminology can only relate to those features specified in said claim and is clear, provided that said features are individually unobjectionable as in this case.

Buffers are not covered by the claims as only the quoted four chloride salts may be present. It is not permitted to read into the amended claims buffer details from the description, in particular from examples, which are now excluded by the claims. During further prosecution it is to be expected that the description will be adapted to the restricted claims.

The term "rinsing" was defined in the description as relating to washing with water (see page 3, line 18 of the patent in suit) and there is no requirement placed upon the quality of the water. Thus, any water as conventionally used for rinsing purposes is suitable for the washing step. This does not lead to any

ambiguity.

The language of paragraphs (c) and (d) of claim 1 is not confusing for the skilled person who would know that a more dilute solution of salts is intended to release impurities first before treatment with a more concentrated solution which elutes the lactoferrin free from the said impurities. What is important is that the concentration of the solution of salts in the lactoferrin desorption step is higher than that of the first treatment to remove impurities thus ensuring a product of high lactoferrin content and this is reflected in the claims. It is not inconsistent to specify two ranges of salt concentrations which overlap provided that the above condition is always met.

Nor is the appellant obliged to calculate purity of the product by a method dictated by the respondents. Laurell's method is known in the art, eg. from D3, and was followed consistently throughout the specification. The skilled person has not been misled or given false information because the results achieved are those indicated by Laurell's method. Whether or not different purity values would be obtained when testing the same products by a different method is immaterial because the reader was instructed to determine purity as described.

The requirements of Article 84 EPC have been met.

4. *Allowability of amendments, Article 123(2) EPC*

4.1 Respondent I did not have any objection to raise under this article of the EPC, while Respondent II indicated

that his comments made in respect of Article 84 EPC above should be considered under this article of the EPC.

4.2 In the board's opinion nothing which the latter respondent said in his statement to the board constituted a sound objection relating to added subject-matter. His arguments are all outlined in the paragraphs above and fail to highlight any single valid reason for discussion pertinent to this question.

4.3 A comparison of the claims of this request with the claims and description of the European patent application as filed leads the board to the following comments:

In claim 1 paragraph (a), the definition of the cation-exchanger haemoglobin adsorbing property has been clarified and more precisely defined by reference to the sodium ion content at 25°C. This amendment was based on the disclosure at page 6 of the application.

The rinsing step of paragraph (b) is more restricted in that the rinsing is now limited to a rinsing means "consisting of water" rather than "washed with water".

The optional washing step (paragraph (c) of the claim) was originally the subject-matter of claim 4 of the application as filed and was not limited in terms of the salt concentration. There is now a restriction to use of a 0,4 to 2,5% solution of any of the four specified salts and this is based on claims 4 and 5 of the European patent application as originally filed.

In the desorption step defined in paragraph (d) of claim 1 there is now a reference to a desorbing means being a salt solution "consisting of one or more salts selected from the group consisting of sodium chloride, potassium chloride, calcium chloride and magnesium chloride" which is narrower than the original form "a solution of one or more salts". Further to this the 80% lactoferrin purity limit has been taken in as well as the salt concentration range 1,5 to 12 wt%. These details of the claimed process were disclosed in claims 3, 4 and 5 of the originally filed application.

The subject-matter of claim 2 appendant to claim 1 is supported by claim 2 of the European application as filed.

The reasoning given above applies also to independant claim 3 of which the 95% lactoferrin purity value is supported by originally filed Example 2.

From the above it is seen that the subject-matter of the claims of the main request complies with the requirements of Article 123(2) EPC.

5. *Allowability of amendments, Article 123(3) EPC*

Neither of the respondents has objected to the amended claims under this provision. Nor can the board see any reason for such an objection because all the claim details were recited in the granted claims and each amendment is of a restrictive nature.

A comparison made between the present claim 1 and claim 1 as granted reveals that the use of the phrase

"consisting of water" in paragraph (b) and the inclusion of the subject-matter from claims 3, 4 and 5 as granted into paragraph (d) of claim 1, are of a limiting nature. The optional washing step now paragraph (c) of claim 1 is derived from claims 4 and 5 as granted and this rearrangement is not objectionable. The subject-matter of claim 2 (appendant to claim 1) is the same as that of claim 2 as granted and claim 3 of the present main request represents a combination of the subject-matter of claims 1 and 3 to 6 as granted. Therefore no amendment has been made which extends the protection conferred and Article 123(3) EPC has not been contravened.

6. *Novelty, Article 54 EPC*

Neither of the respondents objected to the novelty of the subject-matter of the claims now on file.

The board agrees that said subject-matter is novel over the disclosures of D1 and D2.

The process of independent claims 1 and 3 of the patent in suit includes a step of rinsing with water whereas D1 does not disclose such a step. This prior art refers to elution of the CM-sephadex with hydrochloric acid buffer followed by elution to recover lactoferrin again using a buffer mixture of 0.05 M-tris/HCl containing 0.5 M-NaCl. Buffers are not employed in the process as now claimed. Accordingly the claimed process of the patent in suit is distinguished from that of D1.

The subject-matter of claims 1 and 3 of this request is novel over that of D2 because the desorption step in

the process of said document is carried out with a phosphate buffer solution, whereas the claimed process of the patent in suit employs a desorbing means consisting of a solution of one or more of the specified chloride salts, thus phosphate buffers are excluded. Claim 2 of the patent in suit is appendant to claim 1 and accordingly its subject-matter is likewise distinguished from this prior art.

7. The board finds that the new main request satisfies the requirements of Articles 54, 84 and 123(2) and (3) EPC and consequently there is no need to consider the auxiliary request.

8. *Remittal to the first instance, Article 111(1) EPC*

Since the appellant has requested that the case be remitted, to which the respondents agree, and because the first instance did not examine the subject-matter of the patent for inventive step, the board makes use of its power under Article 111(1) EPC to remit the case to the first instance for consideration of the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The subject-matter of the main request is novel.

3. The case is remitted to the first instance for further prosecution of the issue of inventive step.

The Registrar:

The Chairman:

A. Townend

L. Galligani