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Datasheet for the decision of 21 June 2007

Case Number: T 0936/03 - 3.3.08

Application Number: 92307258.1

Publication Number: 0532173

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Language of the proceedings: EN

Title of invention:
Crystalline lactulose trihydrate and a method for its manufacture

Patentee:
MORINAGA MILK INDUSTRY CO., LTD.

Opponent:
INALCO S.P.A.

Headword:
Lactulose trihydrate/MORINAGA

Relevant legal provisions (EPC 1973):
EPC Art. 83, 100(b), 111(1), 114(2)
RPBA Art. 10a(1)(a),(4)

Keyword:
"Sufficiency of disclosure (yes)"
"Remittal to the opposition division (yes)"

Decisions cited:
T 0014/83, T 0226/85

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0936/03 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 21 June 2007

Appellant: (Patent Proprietor)
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Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 26 June 2003 revoking European patent No. 0532173 pursuant to Article 102(1) EPC 1973.**

Composition of the Board:

Chairman: L. Galligani
Members: M. R. Vega Laso
B. Günzel

Summary of Facts and Submissions

I. European patent No. 0 532 173 with the title "Crystalline lactulose trihydrate and a method for its manufacture" was granted on European patent application No. 92 307 258.1, filed on 7 August 1992 and claiming the priority of a previous Japanese application of 9 August 1991. The claims of the granted patent were as follows:

"1. A crystalline lactulose trihydrate having the molecular formula $C_{12}H_{22}O_{11}.3H_2O$, wherein said crystalline lactulose trihydrate has the following physical and chemical properties:

a) elemental analysis (in molar ratio) carbon : hydrogen : oxygen is 12: 28: 14;
b) molecular weight: 396 dalton as determined by the cryoscopic method;
c) moisture content: about 13.6% by weight as determined by Karl Fischer method;
d) starting point of melting: 58 - 60°C as determined by the capillary method; and
e) specific rotation: exhibiting mutarotation but a specific rotation of -43 ± 0.3° as measured at 20°C of 1% by weight of aqueous solution in the equilibrium state.

2. A method for the manufacture of the crystalline lactulose trihydrate of claim 1, comprising the steps of;

concentrating a lactulose syrup, comprising lactulose at a concentration of 70 - 90% by weight of the total

solid matter, to provide a concentrate with a total solids content of up to 65 - 75% by weight and a concentration of lactose in water less than 10% by weight,
cooling the concentrate to a temperature of 2 to 20°C,
seeding with trihydrate crystals of lactulose,
forming the crystalline lactulose trihydrate of claim 1 by stirring, and
separating the crystalline lactulose trihydrate of claim 1."

II. The granted patent was opposed on the grounds of Article 100(a) EPC 1973, in particular lack of novelty (Article 54 EPC 1973) and lack of inventive step (Article 56 EPC 1973). During opposition proceedings, the ground for opposition of Article 100(b) EPC 1973 was introduced and examined *ex officio* by the opposition division.

III. By a decision posted on 26 June 2006, the opposition division revoked the patent under Article 102(1) EPC 1973. In its decision, the opposition division remarked that the patent specification did not indicate the need for "initial" crystallization seed in order to carry out the invention as claimed. Moreover, in the opposition division's view, the proprietor had failed to credibly demonstrate that the lack of teaching in the patent about suitable crystallization seed could have been remedied by the skilled person without undue burden. Consequently, the invention as claimed in the patent (main request) or as defined in any of the auxiliary requests 1 to 6 filed with letter of 27 February 2003, was found not to be disclosed in a manner sufficiently

clear and complete for it to be carried out by person skilled in the art (cf. Articles 100(b) and 83 EPC 1973).

IV. The proprietor of the patent (appellant) lodged an appeal against the decision of the opposition division. In its statement setting out the grounds of appeal filed on 5 November 2003, the appellant submitted, as its main request, claims 1 and 2 as granted. Additionally, six sets of claims identical to those considered by the opposition division when arriving at its decision were submitted as auxiliary requests. The appellant also filed experimental evidence in the form of two declarations (K2 and S2; see section X below), a CD-ROM and a video tape. Two declarations (K2 Suppl. and K3; see section X below) and a CD-ROM were filed by letter dated 7 November 2003.

V. The respondent filed observations on the grounds of appeal and submitted experimental evidence (declaration B4; see section X below) and a video tape. The respondent requested that the declarations K2 and S2 filed by the appellant be disregarded pursuant to Article 114(2) EPC 1973.

VI. In response to the arguments and evidence submitted by the respondent, the appellant filed further evidence (Exhibits A to G).

VII. Additional arguments supported by documentary evidence (Annexes 1 to 7) were submitted by the respondent.

VIII. Since both parties requested oral proceedings under Article 116 EPC 1973 in the event that the board was

not minded to grant their respective requests, the parties were summoned to oral proceedings. In a communication dated 22 February 2007 which was sent under Article 11(1) of the Rules of Procedure of the Boards of Appeal (RPBA) as applicable at that date, the board provided some observations on the evidence filed by the parties on appeal, and drew attention to issues which seemed to be of special significance.

IX. Oral proceedings were held on 21 June 2007.

X. The following documents are referred to in the present decision:

K2: Notarized declaration of Prof. Ulrich Kulozik dated 28 October 2003;

K2 Suppl.: Notarised Supplement to declaration by Prof. Dr. Kulozik (K2), dated 26 February 2004;

S2: Notarised declaration by Dr Sanada dated 28 October 2003;

K3: Notarised declaration of Prof. Ulrich Kulozik dated 26 February 2004;

B4: Certified declaration of Prof. Fabrizio Bruni dated 17 May 2004;

Exhibit A: Copy of page 745 of Merck Catalogue Reagents - Diagnostics - Chemicals, 1990/91;

Exhibit C: Standard Dictionary of the English Language combined with Britannica World Language Dictionary, 1963, Volume 1, pages 548 and 676;

Exhibit D: Letter of Ms Karen K. Amos, Director, Regulatory & HSE Compliance, EMD Bioscience, Inc., dated 22 September 2004;

Annex 2: Y. Liu et al., Journal of Colloid and Interface Science, 1997, Vol. 186, pages 102 to 109;

Annex 3: Enciclopedia della tecnica e della meccanica, ed. F. Rossi and C. Schinaia, page 362, and Enciclopedia della Scienza e della Tecnica, 1964, ed. A. Mondadori, Milan, Italy, pages 642 and 643; English translation of two underlined passages.

XI. The submissions made by the appellant may be summarized as follows:

Admission of new evidence submitted on appeal

The experimental evidence in declarations K2 and S2 had been filed in response to the reasons given by the opposition division in the decision under appeal, and was highly relevant to the issues at hand.

Sufficiency of disclosure

At the relevant date of the patent, crystals of lactulose trihydrate were not available in the art. Thus, the key issue in dispute was whether or not the skilled person was able to produce any initial lactulose trihydrate seed crystals without any undue burden in order to carry out the process of claim 2. How the appellant arrived at the invention was totally irrelevant to the determination of sufficiency. The

assessment of sufficiency was to be made purely on the basis of whether or not a person skilled in the art at the relevant date was able to put the invention into practice making use of the teachings of the patent and common general knowledge.

The person skilled in the art was entirely familiar with methods of crystallization such as the one claimed and, thus, also familiar with the need for an initial crystal. Furthermore, the description (eg. page 3, lines 32 and 34) and claim 2 itself both clearly referred to the need for seed crystals. There was absolutely no prejudice in the mind of the skilled person against the use of anhydrous lactulose seed crystals to crystallize lactulose trihydrate crystals.

In order to practice the invention, the skilled person had to decide which seed crystals to use, and how to use them. With regard to the type of seed crystals, the patent taught that the trihydrate form needed not be used as crystallization seed, but that, preferably, the seed crystals should be those of the trihydrate. Since the anhydrous form was the only form available at the priority date of the patent, the skilled person would inevitably use this form as a seed crystal.

It was important to note that the experiments carried out by the appellant and at least one of the respondent's experiments conclusively showed that some crystals of lactulose trihydrate could be produced using anhydrous lactulose crystals as crystallization seed. Thus, it was an undisputed fact that at least some crystals of lactulose trihydrate could be produced using seed crystals of anhydrous lactulose. With regard

to the question how to use the seed crystals, it was reasonable to expect that the skilled person would start with the methods given in the examples of the patent. The evidence in declarations K2 and S2 showed conclusively that the skilled person was able to obtain crystals of lactulose trihydrate using anhydrous lactulose seed crystals in the method of Example 1 of the patent. No "secret know-how" was given to the laboratories carrying out the experiments in declarations K2 and S2. The anhydrous lactulose used as seed crystal in the experiments was available at the relevant date of the patent. Thus, with the specific guidance from the patent and a minimal number of experiments, a person skilled in the art was able to produce seeds of lactulose trihydrate for use in the method according to the claimed invention.

XII. The arguments put forward by the respondent can be summarized as follows:

Admission of new evidence submitted on appeal

Even though the objection of lack of sufficient disclosure had been raised by the opposition division at an early stage of the opposition proceedings, the appellant chose to file the relevant experimental evidence, in particular declarations K2 and S2, on appeal. The appellant gave no explanation for the late filing of these declarations. Moreover, the experimental evidence in the declarations in question was not relevant, since it failed to support the allegation that lactulose trihydrate crystals could be obtained without undue burden of experimentation by reproducing faithfully the method of Example 1 of the

patent and using anhydrous lactulose crystals instead of lactulose trihydrate as crystallisation seeds.

Sufficiency of disclosure

Saying that something was "preferable" was not per se a disclosure of a specific alternative procedure to obtain the trihydrate seed. There was a complete void of specific information in the patent on how to handle the problem of obtaining trihydrate seed crystals in order to perform the process for the first time. Trying to solve this problem on the basis of the patent was like working in the complete dark. Lactulose trihydrate crystals were the only seed used in the examples of the patent and in the claimed method. Thus, lactulose trihydrate crystals were an essential feature of the invention, and replacing them by other seed crystals was not an obvious measure.

Obtaining highly pure lactulose by crystallization from raw syrups containing several impurities and foreign sugars was far from straightforward. The appellant had not indicated any specific prior art suggesting how to obtain lactulose trihydrate crystals by seeding lactulose solutions with a crystal different from trihydrate. Thus, the "common general knowledge" could in no way supplement the specific information lacking in the patent.

The experiments in the declarations filed by the appellant failed to support its allegations, as they had been carried out using materials and methods not specifically disclosed in the patent and/or unavailable at the relevant date. The lactulose syrup used in the

experiments submitted by the appellant differed in composition from the syrup in the examples of the patent. Moreover, the experiments were carried out under experimental conditions that differed from those disclosed in the patent. Specifically, a discontinuous and intermittent gradient as used in the experiments described in declaration K2 (and K3) was not a "gradual" gradient as described in Example 1 of the patent.

In declarations K2 and S2, 99% pure anhydrous lactulose from Calbiochem was used as crystallization seed. However, this product was not available at the relevant date. The lactulose product commercially available at that date had a different anomeric composition because it was obtained by selective precipitation from aqueous syrups treated with ethanol/methanol. By filing declaration K3, in which Acros Organics lactulose was used as crystallization seed, the appellant indirectly acknowledged that the anhydrous lactulose used in K2 and S2 was not available at the relevant date.

Since at the relevant date anhydrous lactulose crystals were obtained from selective precipitation from aqueous syrups treated with ethanol/methanol, any tests aiming at assessing whether or not lactulose trihydrate could be obtained should use anhydrous lactulose crystallized from alcohols as seed. Declaration B4 showed that by following the teaching of Example 1 using anhydrous lactulose crystals obtained from water/ethanol as seeding crystals, and a continuous and regular decreasing gradient of temperature, no crystallisation was achieved.

XIII. The appellant (patentee) requested that the decision under appeal be set aside and the patent be maintained as granted (main request) or that the case be remitted to the opposition division for further prosecution (auxiliary request).

XIV. The respondent (opponent) requested that the appeal be dismissed (main request) or that the case be remitted to the opposition division for further prosecution (auxiliary request).

Reasons for the Decision

Admission of evidence filed by the parties on appeal

1. The respondent objected to the introduction into the proceedings of new experimental evidence filed with the statement of grounds of appeal, in particular declarations K2 and S2 (see section X *supra*).

2. It follows from Article 10a(4) RPBA as it entered into force on 1 May 2003 - which is applicable to the present case - that everything presented with the statement of grounds of appeal filed pursuant to Article 108 EPC 1973 shall, in principle, be taken into account, without prejudice to the power of the board to hold inadmissible facts, evidence or requests which could have been presented in the first instance proceedings.

3. Declarations K2 and S2 were filed together with the statement of grounds of appeal, and the experimental evidence provided therein was relied upon by the

appellant when setting out the reasons why the decision under appeal was challenged. Contrary to the respondent's allegation, the board does not believe that the new evidence shifts the discussion in a different direction, the essential question remaining the same as in opposition proceedings, namely whether or not a person skilled in the art finds in the patent a clear and complete teaching in respect of crystallization seeds enabling him/her to prepare at least some crystals of lactulose trihydrate in order to carry out the invention as claimed.

4. In the board's view, the declarations in question were filed in direct answer to the findings in the decision under appeal, and the experimental evidence provided therein is, *prima facie*, highly relevant to the question whether or not crystallization of lactulose trihydrate may be achieved using anhydrous lactulose as crystallization seed under the experimental conditions specified in Example 1 of the patent. In fact, the relevance of declarations K2 and S2 was indirectly admitted by the respondent itself who, in support of its objection to the admission of these declarations, raised the question why "*the relevant experimental evidence* [was] *supplied only now*".

5. Thus, in the absence of convincing reasons for disregarding declarations K2 and S2, the evidence provided therein is considered to be part of the appellant's case on which the appeal proceedings are based (cf. Article 10a(1)(a) RPBA).

6. No objections were raised against the introduction of further declarations and documents filed by either

party at later stages of the appeal proceedings. As this further evidence concerned issues raised in connection with the decision under appeal, the board, exercising its discretion under Article 114(2) EPC 1973, decided to admit it as well.

Sufficiency of disclosure (Articles 100(b) and 83 EPC 1973)

7. The decisive question in the present appeal is whether or not the ground for opposition mentioned in Article 100(b) EPC 1973 prejudices the maintenance of the patent, either as granted (main request) or in amended form (auxiliary requests 1 to 6). In order to answer this question, the board must assess whether or not the patent discloses the invention to which it relates in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art without an undue burden of experimentation or any inventive effort.

8. According to the jurisprudence of the boards of appeal (see T 226/85, OJ EPO 1988, 336 and further decisions cited in "Case Law of the Boards of Appeal of the European Patent Office", 5th edition, December 2006, chapter II.A.4), for the disclosure of a patent to be considered sufficient the skilled person must have at his/her disposal, either in the specification or from the common general knowledge available at the relevant date, adequate information leading necessarily and directly towards success through the evaluation of initial failures. Sufficiency of disclosure must be assessed on the basis of the application as a whole and not of the claims alone (T 14/83, OJ EPO 1984, 105).

9. In the present case, the invention as claimed in claim 1 consists in crystalline lactulose trihydrate, a crystalline form of lactulose characterized by its molecular formula ($C_{12}H_{22}O_{11}.3H_2O$) and particular physico-chemical properties (see claim 1, section I *supra*). In claim 2 (see section I *supra*), a method for the manufacture of crystalline lactulose trihydrate using crystals of the same compound as crystallization seeds is claimed.

10. As apparent from the patent specification (see Experiments 1 and 2 on pages 4 and 5 of the patent), lactulose trihydrate differs from anhydrous lactulose - the sole crystalline form of lactulose known in the art at the relevant date of the patent - in its behaviour when solved in water or kept under conditions of high humidity, from which clear advantages for the use of the compound according to the invention arise.

11. The method of claim 2 is exemplified in Examples 1 to 3 of the patent. These examples describe the preparation of crystalline lactulose trihydrate starting from commercial lactulose syrup. First, the lactulose syrup is concentrated and cooled to a temperature of 20°C (Example 1) or 15°C (Examples 2 and 3). Lactulose trihydrate seed crystals are then added to the syrup and the mixture is stirred and cooled gradually to 5°C (Example 1) or 2°C (Examples 2 and 3) over a period of 7 days (Examples 1 and 2) or 4 days (Example 3). At the end of this period, the mixture is centrifuged using a cloth filter to separate the crystals from the liquid phase, and the collected crystals are washed and dried.

12. In the present case, it has not been disputed that, once crystalline lactulose trihydrate becomes physically available, carrying out the method of claim 2 following the instructions given in the examples of the patent is a straightforward task which does not require an undue amount of experimentation or any effort above the ordinary skills of an average practitioner. The objection of lack of sufficient disclosure raised by the opposition division was rather based on the fact that lactulose trihydrate crystals were not available at the relevant date of the patent. The appellant did not dispute this fact.

13. The appellant argued however that, when assessing sufficiency of disclosure for the patent in suit, the disclosure content of the patent should not be restricted to the subject-matter of claim 2, ie. to a method of manufacture using lactulose trihydrate crystals as crystallization seeds, the actual teaching of the patent being broader.

14. In view of the arguments of the appellant and the established jurisprudence of the boards of appeal (see eg. T 14/83, *supra*), the question to be decided is whether or not a person skilled in the art at the relevant date, not having at his/her disposal lactulose trihydrate crystals, finds in the patent **as a whole** adequate information that enables him/her to prepare such crystals without having to embark in painstaking experimentation or apply inventive skills.

The disclosure content of the patent as a whole

15. In the decision under appeal, the opposition division stressed that the patent was completely silent about the (initial) non-availability of lactulose trihydrate crystals and the need for at least some crystals of this compound in order to carry out the method of claim 2. The opposition division also questioned how the appellant prepared the "initial" crystals of lactulose trihydrate.

16. The board does not share the views of the opposition division. When reading the specification of the patent in suit, in particular the statements on page 2, lines 43 to 45 ("*stable lactulose crystals which have water of crystallization (hydrates) have not been disclosed in the literature and were unknown before application of the present invention*"), a skilled person immediately had to become aware of the fact that at the relevant date of the patent, lactulose trihydrate crystals were unknown in the art and, thus, not commercially available. Hence, to a person skilled in the art trying to carry out the invention as claimed, and in particular the method of claim 2, the need for some "initial" lactulose trihydrate crystals disclosed itself.

17. The question of the opposition division as to how the proprietor obtained the initial lactulose trihydrate crystals, is regarded to be immaterial to sufficiency of disclosure. Rather, the decisive questions in the present case are whether or not a person skilled in the art finds in the patent specification - possibly supplemented by the common general knowledge at the

relevant date - adequate information on a suitable crystallization seed available at the relevant date, and whether using this seed the skilled person was able to prepare at least some crystals of lactulose trihydrate from concentrated lactulose syrup.

18. The board is convinced that the required piece of information is found in the passage starting on page 3, line 17 of the patent specification. In this passage, a typical procedure for the preparation of crystalline lactulose trihydrate is described. In particular, lines 31 to 35, which concern the crystallization of lactulose trihydrate from concentrated lactulose syrup, read:

"*Next, the concentrated lactulose syrup is cooled to a temperature of 2 - 20°C,* ***lactulose seed crystals*** *are added, the mixture is stirred and crystals are precipitated out. As low a temperature as possible is desirable for precipitating the crystals, and large crystals are precipitated out with gradual cooling and this is desirable. The lactulose for this seed crystal addition (seeding) is* ***preferably*** *in the form of trihydrate.*" (emphasis added by the board)

19. From this passage of the specification, a person skilled in the art learns that crystallization of lactulose trihydrate from concentrated lactulose syrup may be achieved by adding (any) lactulose crystals, even though lactulose trihydrate crystals are expressly preferred as crystallization seeds. In the board's view, the passage of the patent quoted above provides not only the specific disclosure of lactulose trihydrate crystals, but also the generic disclosure of lactulose

crystals as suitable crystallization seeds for preparing crystalline lactulose trihydrate under the specific experimental conditions disclosed in the patent.

20. From the common general knowledge available at the relevant date, the skilled person undisputedly knew that crystalline lactulose, in particular crystalline **anhydrous** lactulose was commercially available. This is also apparent from the statements on page 2, lines 12 and 13 of the patent. Hence, confronted with the problem of preparing at least some lactulose trihydrate crystals, the logical course of action for the skilled person was to follow the instructions given in the specification and use **anhydrous** lactulose crystals as crystallization seeds. Since anhydrous lactulose was the sole form of lactulose known and available at the relevant date, to proceed with anhydrous lactulose as crystallization seed was a straightforward approach which required neither a considerable amount of experimentation nor the application of inventive skills.

21. The respondent alleged that, in view of both claim 2 as granted and the common general knowledge at the relevant date, a person skilled in the art had to regard the phrase "preferably" in the passage of the patent specification quoted in point 18 above as an obvious mistake devoid of technical meaning. However, in the board's view, neither the patent itself nor the common general knowledge provide a basis for this allegation.

22. The fact that claim 2 of the patent as granted is limited to a specific preferred embodiment does not

contradict the technical disclosure of the patent specification. The passage of the specification quoted above (see point 18) does not leave any doubt that lactulose crystals in general and, specifically, lactulose trihydrate crystals are suitable crystallization seeds for preparing lactulose trihydrate. The fact that claim 2 as granted is directed to the specific embodiment using the preferred crystallization seed, and that this embodiment is also exemplified in the patent, does not invalidate the more general disclosure of the patent specification.

23. It should be noted that an average skilled person, although without profound knowledge of patent matters, is nevertheless familiar with patent documents where a similar situation is often encountered. The skilled person is thus aware of the fact that, for a number of reasons, eg. lack of novelty or lack of inventive step of paticular embodiments, the scope of the claims may be more limited than the overall disclosure of the patent specification, and that very often the claims are restricted to a particularly preferred embodiment. Hence, with this in mind, the skilled person has no reason to suspect an error concerning the phrase "preferably". The respondent's allegation cannot be accepted.

24. Furthermore, the board is unable to see in the various passages of the specification referred to by the respondent any support of its further objection that a person skilled in the art would have not regarded anhydrous lactulose as suitable crystallization seed for preparing crystalline lactulose trihydrate. While a different thermodynamic behaviour of lactulose

trihydrate and anhydrous lactulose crystals when dissolved in water - as indicated in the passage on page 4, lines 50 and 51 of the patent referred to by the respondent -, or differences in the affinity for water between the lactulose trihydrate and the anhydrous compound - as apparent from Table 1 of the patent - may suggest differences in the structure and water content of the respective crystals, these differences alone cannot substantiate a prejudice against the use of anhydrous lactulose as crystallization seed, especially in view of the clear teaching in the passage of the patent specification quoted above in point 18.

25. Nor can the alleged prejudice against anhydrous lactulose as crystallization seed be supported by the Annexes 2 and 3 filed by the respondent (see section X above). In Annex 2, which is a scientific publication concerned with the kinetics of the crystallization of fluorapatite in the presence hydroxyapatite seeds and of hydroxyapatite in the presence of fluorapatite seeds, there is no generally valid statement concerning crystallization using seed crystals other than those of the desired substance, let alone concerning the crystallization of lactulose trihydrate. As for Annex 3, which is a copy of the entry "Crystallization" in two technical encyclopaedias in Italian language, the passages referred to by the respondent read (in the English translation):

"*Sometimes, in order to activate the process of crystallisation, it is usual to add to the supersaturated solution, a little crystal* ***of the desired substance****, working as a crystallisation germ.*"

"*Sometimes the action necessary to provoke crystallysation* [sic] *must be energic, like strring* [sic] *or "seeding" with germs or crystal seeds* ***of the same substance****, previously prepared."*
(The emphasis in the English translation was added by the respondent)

26. The passages quoted above point to the possibility of adding crystals of the same substance as seeds when crystallization of a certain substance is desired, but neither of them describes it as an absolutely necessary condition in every case. Rather, it is apparent from these passages that "sometimes" it is "usual" to add crystals of the same substance, but even vigorous stirring may be sufficient for inducing crystallization.

27. Even less convincing are the respondent's arguments based on an allegedly incorrect adaptation of the description to the claims in examination proceedings before the European Patent Office, or the procedural behaviour of the appellant in proceedings before other patent offices. According to the jurisprudence of the Boards of Appeal of the EPO, solely the disclosure content of the patent supplemented by the common general knowledge available to a skilled person is relevant to the assessment of sufficiency of disclosure within the meaning of Article 100(b) EPC 1973.

28. Summarizing the above, the board concludes that the patent as a whole, and in particular the passage of the patent specification quoted in point 18 above, supplemented by common general knowledge provides a clear and complete teaching of lactulose crystals

available at the relevant date which, according to the patent, are suitable crystallization seeds for obtaining crystalline lactulose trihydrate from concentrated lactulose syrup.

Preparation of lactulose trihydrate using anhydrous lactulose as crystallization seed

29. It was a further matter of dispute between the parties whether or not a person skilled in the art at the relevant date was able to obtain crystalline lactulose trihydrate using anhydrous lactulose crystals as crystallization seeds under the experimental conditions described in the examples of the patent.

30. In the decision under appeal, the experimental evidence previously filed by the proprietor (the present appellant) was considered not to credibly demonstrate that, using anhydrous lactulose crystals as crystallization seeds, lactulose trihydrate could be obtained without an undue amount of experimentation.

31. In appeal proceedings, the appellant filed further experimental evidence in support of its position (see section IV above). Amongst the experiments submitted by the appellant, the experiment of declaration K2 is regarded by the board as convincing evidence that, following the instructions given in Example 1 of the patent, at least some crystals of lactulose trihydrate can be obtained using anhydrous lactulose as crystallization seed, even though the yield is significantly lower (39.0 g vs. 1.34 kg) than when lactulose trihydrate crystals are used to induce crystallization, as described in Example 1.

32. The respondent did not dispute that the experiment of declaration K2 reproduces exactly the experimental conditions in Example 1 of the patent with regard to, *inter alia*, the temperature of the lactulose syrup at the time of seeding (20°C), the ratio of lactulose seed crystals to concentrated lactulose syrup (30 g anhydrous lactulose/10 kg concentrated lactulose syrup), the final temperature of the mixture after the crystallization step (5°C) and the duration of this step (7 days). Nor did the respondent contest the results of the physico-chemical analysis indicating that the crystals obtained were crystalline lactulose trihydrate.

33. However, the respondent questioned the probative value of the experiment of declaration K2 pointing to differences in the composition of the lactulose syrup from which lactulose trihydrate was crystallized and in the temperature profile during the crystallization step. The respondent also contended that the anhydrous lactulose crystals used as crystallization seeds in the experiment of declaration K2 differed from those available at the relevant date of the patent. In the following, these issues will be discussed in detail.

34. It is in fact apparent from the results of the analysis of the lactulose syrup used as starting material in the experiment of declaration K2 (see K2 Suppl.; section X above) that both the solid matter content of the concentrated lactulose syrup, and the lactulose and galactose contents in solid matters of the initial syrup deviate slightly from the values given in Example 1 of the patent (68.9% vs.71.5% for the solid

matter content, 74.7% vs. 73.5% for the lactulose content and 12.2% vs. 10.7% for the galactose content in solid matters). However, as far as the solid matter content after concentration of the syrup and the initial lactulose content are concerned, the extent of the deviation from the values in Experiment 1 is within the usual experimental margin of error, and not greater than in the corresponding experiment of declaration B4 submitted by the respondent (see section X above), where solid matter content and lactulose content of the syrup amount to 72.13% and 72.4%, respectively. As for the galactose content in the initial lactulose syrup, neither the patent nor any of the documents on file address its relevance to the crystallization of lactulose trihydrate, and no arguments have been put forward by the respondent in this respect.

35. In respect of the respondent's objection concerning the temperature profile during the crystallization step in the experiment of declaration K2 (see section XI above), the board notes that neither in Example 1 nor anywhere in the patent is there a requirement for a linear temperature management during the crystallization step. Rather, it is stated in Example 1, in particular in the passage on page 6, lines 29 and 30 that "...*the mixture was cooled* ***gradually*** *over a period of 7 days to 5°C ...*"(emphasis added by the board). Since the patent specification does not provide more detailed instructions how the cooling step is to be performed, the term "gradually" in the passage quoted above must be construed as it was understood by a person skilled in the art, namely as "proceeding by steps or degrees; moving or changing slowly or regularly; slow" (see Exhibit C; section X above). In the board's view,

cooling the mixture of concentrated lactulose syrup and anhydrous lactulose crystals from 20°C to 5°C in 2°C steps over 7 days - as in the experiment of declaration K2 - amounts to a slow, step by step reduction of the temperature of the mixture, ie. to a "gradual cooling" as described in Example 1 of the patent. Hence, the respondent's argument cannot be accepted.

36. Finally, the respondent disputed that the anhydrous lactulose crystals used as crystallization seeds in the experiment of declaration K2 were available at the relevant date of the patent. In this experiment - as well as in the experimental evidence filed by either party in opposition proceedings -, concentrated lactulose syrup was seeded with lactulose crystals purchased from Merck Calbiochem.

37. In response to this objection, the appellant submitted a copy of a letter from EMD Bioscience, Inc, the supplier of Calbiochem's lactulose (see Exhibit D, section X above). In this letter, EMD Bioscience, Inc certified that it had been supplying lactulose purchased from Merck KGaA since September 1999, and that prior to that date this product was supplied by Merck under the catalogue number 5283 (see Exhibit D; section X above). This latter point is confirmed by Exhibit A, which includes a copy of page 745 from Merck's Reagents, Diagnostics and Chemicals Catalogue 1990/1991 listing lactulose under catalogue number 5283. The evidence provided in Exhibits D and A has not been questioned by the respondent, and the board sees no reason to do it on its own motion.

38. Thus, in view of the evidence in declaration K2 and Exhibits A and D, the board considers that the appellant has discharged the burden of proof concerning its assertion that, at the relevant date of the patent, a person skilled in the art was able to crystallize lactulose trihydrate using commercially available lactulose crystals as crystallization seeds under the experimental conditions specified in Example 1.

39. This finding is not affected by the respondent's further objection that only experiments using as seed crystals anhydrous lactulose crystallized from alcohols could be regarded as convincing evidence, because the Merck Calbiochem's lactulose available at the relevant date – other than the product used in the experiment of declaration K2 - was prepared by selective precipitation from aqueous syrups treated with ethanol/methanol and, consequently, had a different anomeric composition.

40. The respondent argued that, in 1991, crystallization using alcohols was the sole method known and currently used for the preparation of anhydrous lactulose, and referred in this respect to the overview of the state of the art on page 2 of the patent specification. However, in the board's view the cited passage of the specification (see page 2, lines 14 to 37) fails to support the respondent's allegation. It is apparent from this passage that, besides methods for the crystallization of lactulose using alcohols, also other crystallization methods were known in the art, in particular methods which did not use alcohols. Hence, in view of this evidence there is no reason to assume that the Merck Calbiochem's lactulose available at the

relevant date was necessarily anhydrous lactulose crystallized with alcohol.

41. Consequently, whether or not Merck Calbiochem's lactulose as presently on the market and anhydrous lactulose crystallized from water/ethanol have a different anomeric composition, as shown in declaration B4 submitted by the respondent, has no bearing on the finding above. The same applies to the further experimental evidence in declaration B4 which aims at showing that crystallization of lactulose trihydrate cannot be effected using anhydrous lactulose crystallized from water/ethanol as crystallization seeds under the conditions specified in Example 1 of the patent.

42. Summarizing the above the board concludes that, having regard to evidence presented by the appellant on appeal, the requirement of sufficiency of disclosure is fulfilled with respect to the claims of the main request (claims as granted). Thus, since for this reason the decision under appeal must be set aside, there is no need to examine auxiliary requests 1 to 6 filed by the appellant on appeal.

Remittal to the opposition division

43. Even though the opposition division indicated in its decision that, as a conclusion, novelty and inventive step could be recognized, it is clear from the absence of any reasoning as to why the claimed subject-matter would be novel and inventive, that a final decision in this respect cannot be regarded as having yet been given by the oppositon division. Therefore, the board,

exercising the discretion to which it is empowered by Article 111(1) EPC 1973, remits the case to the opposition division for further prosecution, thereby granting the auxiliary requests of both parties.

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 for further prosecution.

The Registrar: The Chairman:

A. Wolinski L. Galligani