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D E C I S I O N
of 15 May 1999

Case Number: T 0644/96 - 3.3.4

Application Number: 88100359.4

Publication Number: 0318630

IPC: C07H 3/04

Language of the proceedings: EN

Title of invention:

Method for preparing high purity cristalline lactulose and the product obtained

Patentee:

Inalco S.p.A.

Opponent:

Laevonsan-Gesellschaft m.b.H.
Aono Michiyo
Duphar International Research B.V.

Headword:

High purity crystalline lactulose/INALCO

Relevant legal provisions:

EPC Art. 83, 100(b)

Keyword:

"Sufficiency of disclosure (no)"

Decisions cited:

T 0226/85

Catchword:

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Boards of Appeal

Chambres de recours

Case Number: T 0644/96 - 3.3.4

D E C I S I O N
of the Technical Board of Appeal 3.3.4
of 15 May 1999

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Decision under appeal:

**Decision of the Opposition Division of the
European Patent Office posted 17 May 1996
revoking European patent No. 0 318 630 pursuant
to Article 102(1) EPC.**

Composition of the Board:

Chairman: U. M. Kinkeldey
Members: D. D. Harkness
W. Moser

Summary of Facts and Submissions

I. European patent application No. 88 100 359.4 having the title "Method for preparing high purity crystalline lactulose and the product obtained" was granted as European patent 0 318 630 with claims 1 to 8 for all member States except ES and GR, and with claims 1 to 7 for ES and GR. The main claim was the same for all designated States. This claim read as follows:

"1. A method for preparing crystalline lactulose having less than 2% of carbohydrates other than lactulose and a purity exceeding 98%, characterized by crystallizing an aqueous solution having the following characteristics:

- a) lactulose concentration of 50-80% w/w in the aqueous solution;
- b) lactose concentration of less than 5% of the lactulose concentration by weight;
- c) galactose concentration of less than 5% of the lactulose concentration by weight;
- d) concentration of other carbohydrates of less than 4% of the lactulose concentration by weight."

II. The patent in suit was revoked by the opposition division because it did not disclose the invention in a manner sufficiently complete for it to be carried out by a person skilled in the art, (Article 100(b) EPC). An essential element for carrying out the claimed process was to have crystalline lactulose seed crystals at hand to trigger crystallization according to the claimed process. Respondent I (opponent 01) had shown by experimental data that by using seed crystals

available to the public before the priority date of the patent in suit no crystallization as claimed took place. It was years after said priority date that document (6) showed how to prepare the necessary lactulose seed crystals. The description of the patent in suit was completely silent concerning what to do in order to obtain the required seed crystals. The appellant (patentee) had admitted that said lactulose crystals necessary for carrying out the further crystallization steps was obtained by chance.

- III. The appellant lodged an appeal, paid the appeal fee and filed a statement of grounds in due time.

Respondents II and III (opponents 02 and 03) replied to the appeal. Respondent I withdrew its opposition in a letter filed on 30 July 1998.

- IV. The appellant argued essentially as follows:

In the art in question it was common general knowledge that, in order to precipitate a crystal of a substance from a solution thereof, it was necessary to use a seeding crystal of the desired product which had been obtained from a solution of said product in the same solvent as it was proposed to precipitate the product from. Thus, in order to prepare crystals from an aqueous solution, the seeding crystal had to be precipitated from aqueous media.

However, the invention did not concern the production of a seed crystal because the real technical teaching of the invention was that "aqueous solutions of lactulose" may be used for crystallization processes,

and thus a technical prejudice which was that lactulose could only be successfully precipitated from alcoholic solutions had been overcome. It was not required that a particular lactulose crystal form should be produced. The aim of the invention was thus to produce a purified lactulose starting from an impure commercially available syrup of lactulose which is defined in the main claim.

Since the skilled person knew that a seed crystal needs to be obtained from an aqueous medium, then all he would have to do was to prepare a saturated solution of the substance in water and wait for crystallization to happen, and if it did not occur in a conventional period of time, then no real burden was put upon him to wait a longer period of time to see if precipitation did in fact take place.

Once the skilled person had obtained a seed crystal from aqueous solution, then this may be used in the process which was essentially characterised by the defined aqueous starting solution.

Experimental evidence in support of the appeal was filed.

V. The respondents' arguments may be summarised as follows:

The respondents agreed with the appellant that only seed crystals obtained from aqueous solutions may be used in the process of the invention. However the patent in suit did not disclose anywhere how such seed crystals may be obtained.

The only seed crystals available at the priority date had been obtained from alcoholic solutions, and they dissolved in the aqueous lactulose solution without initiating the crystallization process as demonstrated by experimental data.

The experimental results showed that seed crystals obtained from alcoholic solutions did not initiate crystallization from aqueous solutions, and it was only possible to carry out this process using seeds of lactulose trihydrate, first recognised in 1992, ie many years after the priority date of the patent in suit.

It had been admitted by the appellant that the seed crystals used were obtained only **by chance** after an aqueous solution of lactulose had been left to stand for a few months, thus the appellant did not know enough about how to produce them or their identification and was unable to give the required details in the patent in suit, which however was indispensable for carrying out the claimed process.

The respondents criticised the technical evidence filed by the appellant in that the experiments did not comply with the process conditions set out in the description of the patent in suit, ie, crystallization times and temperatures. Thus the process was unworkable, and the patent disclosure consequently insufficient.

VI. The appellant requested that the decision under appeal be set aside and that the patent be maintained as granted. Oral proceedings were not requested.

The respondents requested that the appeal be dismissed.

Respondents II and III requested oral proceedings in the event that the Board had the intention to reverse the decision under appeal.

Reasons for the Decision

1. The appeal is admissible.
2. The only issue to be dealt with in this decision is sufficiency of disclosure (Articles 83, 100(b) EPC).
 - 2.1 Article 83 EPC requires that a European patent must disclose the invention in a manner sufficiently clear **and complete** for it to be carried out by a person skilled in the art.

It follows therefrom that, in the present case, the disclosure must enable the skilled person to perform the process claimed, and therefore the patent in suit has to indicate all the technical details which would allow successful carrying out of the process.

- 2.2 It is accepted in the art, and the appellant does not deny, that in order to precipitate a crystal form of a substance from a solution of said substance, then a seed crystal of said substance in said form has to be added to the solution to initiate precipitation. The seed crystal necessarily has to have been produced from a solution of the desired product in the solvent from which it is intended to carry out precipitations according to the inventive method. Therefore, such a seed crystal must have been made available to the public.

2.3 Thus, the question to be answered is whether or not the skilled person was advised by the specification of the patent in suit or, at the time of the priority date of the patent in suit, would have known by applying common general knowledge how to produce a seed crystal from aqueous solution without any undue burden being placed upon him. In this context, experimentation involving a reasonable amount of trial and error would be acceptable according to the established case law of the Boards of Appeal (see e.g. decision T 226/85 OJ EPO 1988, 336).

2.4 The patent in suit mentions the lactose seed crystals necessary to trigger crystallization according to the process claimed three times, namely in examples 1 to 3, without one single word of how to obtain them. Thus, the skilled person is left without **any** information in the patent in suit how to overcome any difficulties in preparing the seed crystals of lactulose, let alone that it may take possibly up to four months to get them and thus the entire burden of the preparation of this essential component of the claimed process is placed on the public. Thus, the Board has to examine whether the skilled person at the priority date of the patent in suit would have been able to produce the essential lactulose seed crystals by applying common general knowledge without undue burden. The appellant has submitted experiments and arguments to support his contention that this was so.

2.5 In order to show that the seed crystals can be produced by a skilled person using only common general knowledge, experiments were filed by the appellant on

11 September 1996. These experiments do not support his case because as presented they employ solutions of lactulose crystals obtained by crystallization from ethanol as described in US-A-4 536 221 in aqueous media (experiment 1) and in aqueous/alcoholic media (experiment 2), and either no seed crystal at all or an undefined seed crystal is used to precipitate lactulose. According to the experiments "the solutions were cooled to room temperature and subjected to crystallization", but again, the crystallization process has not been fully described. This is also contrary to the accepted practice that only a seed crystal obtained from aqueous media would be suitable for precipitation from an aqueous medium. The Board does not agree with the appellant's statement (cf. letter dated 20 March 1997) that the products of tables 1 and 2 (experiments) correspond with those of examples 2 and 3 of the patent in suit because the said tables refer to seed crystal production and the examples to the product lactulose of the process according to the invention. Further, there are differences between the processes which provide a crystal to be used as a seed crystal in the process of invention and the process for crystallization of the lactulose product, which are that all but one of the tests performed in the experiments (table 2, test 2) required a time for crystallization well above the 60 hours limit set by the process of the patent in suit and seven out of nine cooled to 4°C rather than 5°C (page 3, lines 31 to 32). Table 2, test 2 employed a solvent mixture of 105 g of water with 297 g ethanol which is a predominantly alcoholic solvent.

The Board does not agree to the view (cf. appellant's letter filed 21 March 1997, page 3) that to effect a seed crystallization from aqueous media would be evident to a skilled person if he then afterwards wished to precipitate lactulose according to the process of the invention. This course of action still begs the questions of how to obtain the seed crystal from aqueous media, and whether an aqueous medium should be used to be successful.

The argument that in the case that both the seed crystal and the further production of crystallized lactulose may be produced by the same process, and therefore one process defines production of seed crystal and final product, thereby overcoming the insufficiency objection, is not accepted by the Board because there was no statement in the patent in suit that the process was carried out to prepare seed crystal and then repeated using said crystal to perform the process of claim 1. Further, the appellant stated in the letter filed 21 March 1997 on page 4 that "the problem of the industrial process and the problem of seeds are different problems to be solved in different manners".

The appellant's view that no undue burden is placed upon the skilled person seeking a seed crystal, because all that he has to do is dissolve lactulose in water and then wait for precipitation without doing anything else, is not accepted by the Board because this modus operandi, although simple, is uncertain in outcome and bereft of any technical activity which would positively influence seed crystal precipitation.

In this appeal, there was no rebuttal by the appellant of the technical evidence filed by respondent I who unsuccessfully used seed crystals precipitated from alcohol available at the priority date of the patent in suit to carry out the process exemplified in that patent.

The appellant did not indicate (cf. letter filed 21 March 1997, page 6) which teaching in the patent in suit gave the skilled person to believe that a very long seed crystallization time was to be expected, thereby suggesting that sufficient information was given to prepare seed crystal. In the Board's opinion such information does not even implicitly appear in the patent in suit.

2.6 The appellant's argument (cf. letter filed on 21 March 1997) that the invention lies in the use of a commercially available syrup of lactulose to prepare pure lactulose, and that seed crystal preparation was the result of a mere recrystallization of available crystals of lactulose by cooling a super-saturated aqueous solution thereof, is not accepted by the Board because this is an oversimplification of the technical situation. Had it been possible to do that, then there was not a prejudice to overcome, namely that it was previously thought that lactulose could only be successfully precipitated from alcoholic solutions.

2.7 The main claim refers to "crystallizing an aqueous solution" as specified, there being no reference to a seed crystal at all, nor is there any reference to the critical values (cf. patent in suit, page 3, lines 27 to 32) which appear to be essential to the process.

Since the description of the patent in suit specifies only "crystalline lactulose" as seed crystals, there is no guidance given with respect to the production of a suitable seed crystal which alone enables the process to be carried out. In the opinion of the Board such guidance is necessary in this case, especially as the appellant himself declared that to employ aqueous solutions was a departure from the previously established procedures. It was therefore incumbent upon him to establish and disclose a method for seed crystal production in aqueous media.

2.8 It is not acceptable for the purposes of sufficiency of disclosure where it depends on common general knowledge and the patent in suit relates to what is essentially a new technical development, i.e., crystallization of lactulose from aqueous media, to merely say that the skilled person would have no difficulty in producing a seed crystal simply by dissolving lactulose in water and then waiting for crystallization to happen. For those who may try it may not happen at all or only within a time period (4 months) which would have caused the skilled person, who was unaware that it may take that long, to give up. Indeed it appears that the appellant has tried on occasion without success as it was admitted by him that a seed crystal was obtained only by chance. As it was by chance, then the appellant did not know how to get it directly, and it cannot be assumed that the average skilled person would have been able to produce seed crystals from aqueous solvents.

2.9 Accordingly, the lack of technical details with respect to seed crystal production has resulted in an undue burden being placed upon the person skilled in this

art. Nor does it appear reasonable to assume the skilled person would succeed using trial and error methods as it would also only be by chance that a seed crystal would be produced. Therefore the process as claimed is not enabled by the disclosure which is insufficient.

- 2.10 The fact that respondent I has withdrawn its opposition (see section III above) for the reason that it has verified the experiments filed by the appellant cannot alter the above finding by the Board on sufficiency of disclosure because the Board does not doubt that the experiments are correct, but believes that the method of carrying them out was beyond common general knowledge and, since such a method was not disclosed in the application as filed, an undue burden was placed on the skilled person.
- 2.11 Referring to an Office Action of the USPTO dealing inter alia with the issue of sufficiency of disclosure, the appellant further submitted that, in order to prove that a claimed process was inoperable, it had to be established that none of its embodiments or examples disclosed in the application as filed was operable. From the above findings (cf. in particular points 2.4 to 2.10) it follows that, in the Board's judgement, this is true in the present case.
- 2.12 Only the respondents II and III have requested oral proceedings, and since this decision is in their favour no oral proceedings are necessary.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairwoman:

U. Bultmann

U. Kinkeldey