

Internal distribution code:

- (A) [] Publication in OJ
(B) [] To Chairmen and Members
(C) [X] To Chairmen
(D) [] No distribution

**Datasheet for the decision
of 23 June 2010**

Case Number: T 0945/09 - 3.3.02

Application Number: 97950310.9

Publication Number: 0946221

IPC: A61K 31/495

Language of the proceedings: EN

Title of invention:

Use of taurolidine or taurultam for the prevention and the treatment of infections in delivery systems

Patentee:

Ed Geistlich Söhne AG Für Chemische Industrie

Opponent:

TauroPharm GmbH

Headword:

Taurolidine in delivery systems/GEISTLICH

Relevant legal provisions:

EPC Art. 54

Relevant legal provisions (EPC 1973):

-

Keyword:

"Novelty (no): Public prior use"

Decisions cited:

T 1057/92

Catchword:

-



Case Number: T 0945/09 - 3.3.02

DECISION
of the Technical Board of Appeal 3.3.02
of 23 June 2010

(Opponent) TauroPharm GmbH
Mit Sitz in Würzburg
Jägerstr. 5a
D-97297 Waldbüttelbrunn (DE)

Representative: Andrae, Steffen
Andrae Flach Haug
Balanstrasse 55
D-81541 München (DE)

Respondent: Ed Geistlich Söhne AG Für Chemische Industrie
(Patent Proprietor) Bahnhofstrasse 40
CH-6110 Wolhusen (CH)

Representative: Barry, Robert Stewart Wilson
Central Court
25 Southampton Buildings
London WC2A 1AL (GB)

Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 2 April 2009
rejecting the opposition filed against European
patent No. 0946221 pursuant to Article 101(2)
EPC.

Composition of the Board:

Chairman: U. Oswald
Members: H. Kellner
J. Van Moer
J. Riolo
J.-P. Seitz

Summary of Facts and Submissions

- I. European patent No. 946 221, filed as application No. 97 950 310.9 based on international application PCT/GB1997/003524 and published as WO 1998/028027, was granted with seven claims.

Claim 1 as granted reads as follows:

"Use of taurolidine or taurultam in the manufacture of a solution for preventing or reducing infection and sepsis

in or caused by a delivery system for administration of a desired liquid material to a patient or withdrawal of a blood sample from a patient,

wherein said solution is employed to fill the system between each said administration or withdrawal

so as to act as an antimicrobial seal serving to prevent or reduce said infection and sepsis."

- II. Opposition was filed against the granted patent by the appellant. The patent was opposed under Article 100(a) EPC for lack of novelty and lack of inventive step and under Article 100(c) EPC because it contained subject-matter which had not originally been disclosed.

The following documents *inter alia* were cited during the proceedings before the opposition division and the board of appeal:

- (1) D.A. Johnston et al.; Clinical Nutrition; 1993, vol. 12, 365-368
- (2) J.I. Blenkarn; Clinical Nutrition; 1987, vol. 6, 35-38
- (3) B. Jurewitsch et al.; Journal of parenteral and enteral nutrition; 1998, 242-244
- (4) M. M. Mughal; Br. J. Surgery; 1989, 76(1), 15-21
- (7) B. Messing et al., "Antibiotic-lock technique: A new approach to optimal therapy for catheter-related sepsis in home-parenteral nutrition patients", Journal of parenteral and enteral nutrition; 1988, vol. 12(2), 185-189
- (14) Copy of letter dated 7 February 1996 from Mr Pfirrmann (Ed. Geistlich Söhne AG) to Mr Jurewitsch filed by the respondent with letter dated 14 November 2007
- (20) List of shipments of taurolidine from Geistlich to Mr Jeejeebhoy (document 20a) and four authorisation letters (1996-97) (documents 20b, c and d) filed by the respondent with letter dated 20 November 2008
- (25) Further correspondence (dated 24 January 1997, 12 March 1997 and 17 March 1997) between Mr Pfirrmann, Mr Jeejeebhoy and Mr Jurewitsch filed by the respondent with letter dated 20 November 2008

(27) B. Messing et al.; Clinical Nutrition, 1990,
Vol. 9, 220-225

III. The appeal lies from the decision of the opposition division under Article 101(2) EPC, pronounced at oral proceedings on 20 January 2009 and posted on 2 April 2009.

The opposition division held that none of the grounds of opposition prejudiced the maintenance of the European patent and that therefore the opposition was rejected.

With respect to Article 100(c) EPC, the opposition division considered that, taking into account the passage bridging pages 6 and 7 of the application as originally filed, this ground did not *prima facie* prejudice the maintenance of the patent.

As far as Article 100(a) novelty is concerned, the opposition division concluded that on the basis of the information reported in document (3) the use of 2% taurolidine solutions to fill catheters started before the priority date of the contested patent, in a time-frame which spanned July 1995 and October 1996, depending on whether the date when the article was submitted or finally published was taken into account. This use occurred before the priority date.

However, the opposition division also concluded that all information concerning the use of taurolidine as catheter lock available to the acting medical team, to the patent proprietor (supplier of taurolidine) and to the patient was covered by an implicit obligation of

confidentiality which stemmed from the specific circumstances of the case.

In this situation the burden of proof was upon the opponent to establish that no implicit obligation of confidentiality existed, or that notwithstanding this obligation the invention was disclosed to the public. The opponent had not discharged this burden.

Therefore, the opposition division arrived at the conclusion that the evidence provided in the course of the proceedings was not sufficient to establish that the claimed invention was rendered available to the public in such a way that it was comprised in the state of the art.

Since the opponent had withdrawn the novelty objection based on documents (1) and (2), and since the opposition division did not consider these documents to *prima facie* prejudice the novelty of claim 1, the division did not maintain or reintroduce this objection in the proceedings of its own motion.

In particular, in view of document (27) as closest prior art in combination with documents (4) or (1) or (2), the subject-matter of claim 1 also involved an inventive step.

Thus, the opposition was rejected.

IV. The appellant (opponent) filed an appeal against that decision and submitted grounds of appeal.

V. On 23 June 2010, oral proceedings took place before the board.

VI. The submissions of the appellant can be summarised as follows:

From the teaching of document (3) a Canadian medicinal team clearly had used an embodiment of claim 1 of the patent in suit, the taurolidine-lock technique, beginning in summer 1995. This was affirmed by document (25) which was introduced by the respondent during the proceedings before the opposition division.

This teaching was used during treatment of a patient by the patient himself while having home parenteral nutrition (HPN).

No implicit obligation of confidentiality with respect to the use of taurolidine in a lock solution before the priority date of the patent in suit could be inferred from the evidence in the proceedings or from the jurisprudence in the medicinal field. In addition, the respondent had not claimed any explicit agreement on confidentiality, established between the respondent and the authors of document (3) either in writing or orally, although it should have been easy for him and no undue burden to provide evidence for such an agreement.

Generally, the published teaching could not really be challenged by merely questioning the content of a duly printed article and its disclosure by submitting unsubstantiated indicia depending on mere assumptions that things could have happened in another way.

Therefore, the teaching of claim 1 of the patent in suit was not new with respect to document (3).

VII. The respondent's arguments as to public prior use of the subject-matter of the patent in suit related to three main topics and may be summarised as follows:

- (a) The appellant, although burdened with the proof of the alleged prior use, had not met the standards for a chain of evidence and arguments on the basis of the balance of probability that was necessary for accepting a novelty-destroying prior use to be established.

There was an inevitable reasoning based on the episodes of the treated patient's illness, on his age to be derived therefrom and additionally on the evidence submitted in connection with shipments of taurolidine to the Canadian scientists that the treatment of the patient with a taurolidine-lock had not begun before March 1996.

In addition, there was evidence from document (3) that this treatment at least at the beginning was accompanied by systemic therapy with vancomycin. From the quantities received by the hospital it could even be inferred that taurolidine was probably administered in parallel as an additive to the nutritional solution (Ninewell's method).

Accordingly, there was a late update of the report in document (3) when the "new tunnelled subclavian" was active for 12 months, i.e. 10 plus 12 months after March 1996, in other words

January 1998, six months before publication in July 1998. Amendments after the receiving or accepting date were not unusual in the journal of publication (3), as could be seen from the example and time frames in document (7). The late update was done quite easily by simply adding the last line to table 1.

Consequently, to figure out when the treatment began, it was not possible to start with the date "Received for publication, May 28, 1997" or "Accepted for publication, November 18, 1997".

This reasoning at least threw doubt on the alleged prior use as based on conclusions drawn from document (3) by the appellant. Thus, the existence of the prior use with respect to the questions "what was done" and "when was it done" could not be acknowledged beyond any reasonable doubt.

- (b) With respect to the question of "what was known **to the public**" before the priority date, the appellant had not even tried to provide evidence that the facts as set out in document (3) and consequently any relevant feature of the teaching of the patent in suit were known to the patient himself, let alone any other public person.

As far as "confidentiality" was concerned, the use of the taurolidine-lock constituted at least an entirely experimental use of a medicament that by settled jurisprudence of the boards of appeal was connected to an inherent obligation of confidentiality. In particular, this could be

derived from decision T 1057/92 of 23 January 1997 (not published in the Official Journal).

In addition, on the basis of the two techniques known before the priority date, namely "Ninewell's method" comprising continuous application of taurolidine during parenteral nutrition and the ALT method (using highly dosed antibiotic as the locking fluid during the break between nutrition), the subject-matter of the patent in suit was no simple substitution of antimicrobial fluids which nobody would have thought to be worth keeping confidential.

Finally, since it was clear from the evidence filed by the respondent that use of the taurolidine-lock had not begun before March 1996, and since this had occurred after the correspondence between Mr Pfirrmann, an employee of the respondent and Mr Jurewitsch, one of the Canadian authors of document (3), this use entirely depended on the know-how and support of the respondent, which enforced the confidentiality imposed on all actions taken. Evidence for this communication had been supplied by the respondent as document (14).

- (c) Not everything the authors of document (3) could have done and known before the priority date of the patent in suit had been established as a successful technical method.

They only were beginning to try anything to help a patient in need of some therapy while suffering

repeated catheter-related bloodstream infections (CRBSIs) with no explanation of their origin.

Whether this action or any other accompanying administration of antibiotic or antiseptic substances led to success in treating this single - and therefore statistically irrelevant - patient was not known and at that time could not possibly be seen.

Consequently, even if the information to be derived from document (3) was clearly disclosed, it was far from an established teaching capable of constituting prior use.

VIII. The appellant (opponent) requested that the decision under appeal be set aside and that the European patent be revoked.

IX. The respondent (patentee) requested that the appeal be dismissed.

Reasons for the Decision

1. The appeal is admissible.
2. *Article 100(c) EPC (added subject-matter)*

The subject-matter of claim 1 of the request may be derived from claim 1 in connection with page 6, line 30, to page 7, line 17, of the application as originally filed.

3. *Article 54 EPC (novelty)*

3.1 In one of the alternative embodiments the claimed subject-matter of the patent in suit relates to

- the use of taurolidine in the manufacture of a solution
- for preventing infection and sepsis
- in a delivery system for administration of a desired liquid material to a patient,
- wherein said solution is employed to fill the system between each said administration
- so as to act as an antimicrobial seal
- serving to prevent said infection and sepsis.

3.2 Document (3) teaches

- the use of taurolidine in the manufacture of a solution (page 243, left column, line 4)
- for preventing infection and sepsis (page 243, left column, lines 1 to 3)
- in a delivery system for administration of a desired liquid material to a patient (abstract, left column, lines 3 to 6, in connection with abstract, bridging sentence from left column, last line, to right column, line 3),

- wherein said solution is employed to fill the system between each said administration (abstract, bridging sentence from left column, last line, to right column, line 3, together with page 243, left column, lines 4 to 8)

- serving to prevent said infection and sepsis (page 243, left column, lines 1 to 3, together with page 243, right column, lines 6 to 9).

The person skilled in the art of total parenteral nutrition at the priority date of the patent in suit knows that the catheter lumen must be sealed during times when it is not used for administration of the nutrient, and refers to it as the lock-technique. This seal may be performed using heparin solution as is referred to in document (3), page 243, left column, lines 3 to 4, together with page 243, left column, lines 8 to 9.

Thus, the remaining feature

- so as to act as an antimicrobial seal

is also inevitably comprised in the teaching of document (3).

Consequently, the teaching of document (3) in the form of the reported use of taurolidine solution as a lock represents all the features of claim 1 of the patent in suit.

3.3 Concerning the question of when this teaching of taurolidine-lock was performed, and in particular when it began to be performed, there is *prima facie* the clear-cut normal case that a paper is ready before it is sent to a journal for publication and there is normally no need for substantial amendments after the date of receipt. First there is the record of a success, then the idea and realisation of publication follow. In the current case there is evidence for the particular date of receipt at the bottom of page 242 of document (3), left column: "Received for publication, May 28, 1997".

Since any decision to publish a paper inevitably must lie in the period before its receipt for publication, the authors of document (3) must have decided to publish their experience in the time before May 1997. Following the time frame proposed by the respondent, this would have been just shortly after they had removed the catheter and implemented systemic antibiotic treatment (ten months after March 1996, which was January 1997) - stripped of the experience of a further 12 months free of infection.

According to these considerations, the board is satisfied that the starting date for the use of the taurolidine-lock can be set at 22 months before the date of receipt for publication, i.e. July 1995.

Doubting this normal sequence of actions, under the circumstances of the current case as set out, requires tangible evidence and not just one example of differing experience in another case and statements based on several mere assumptions (see e.g. following point 4.2

of this decision). The maxim "*reus in excipiendo fit actor*" applies here. The burden is on the respondent to show that the actual facts and their sequence in truth were different.

- 3.4 In document (3) it is pointed out that "Ten months before the last infection, the patient was instructed to instil 1.5 mL taurolidine 2% daily into his central line after finishing his HPN (home parenteral nutrition) infusion and has continued to do so 2 years to date" (parenthesis inserted by the board).

Thus, the teaching according to claim 1 of the patent in suit was used by a patient while having "home parenteral nutrition" (HPN). Such a patient, aged around 30, after his long history of complications leading to multiple replacements of the catheter (see document (3), page 242, right column, first paragraph, in particular the last two sentences) usually knows what is happening to him and he is interested in the nature of all actions intended to bring him relief. In addition, the "evaluation of the patient's protocol of site care" mentioned in document (3) (see page 242, right column, last paragraph, lines 3 to 7) would not have been possible without exact explanation for instance of the purpose of the daily instillation of 1.5 mL of heparin solution. Consequently, it is also to be seen as a prerequisite that the intention connected with the heparin replacement by 1.5 mL of taurolidine solution (see page 243, left column, lines 3 to 8) was sufficiently explained to him.

In addition, there is no remark in document (3) indicating anything to the contrary.

Therefore, the board has to base its considerations and conclusions on the knowledge of the patient being clear and concise enough that he could take notice of the technique used after replacement of heparin-lock by taurolidine-lock, representing the teaching of claim 1 of the patent in suit.

There was also no reason for him to treat this knowledge as a secret, because at that time the acting doctors simply tried to apply taurolidine of whatever provenance using a technique they derived freely and easily from the state of the art common to them at that time (see document (3), page 243, right column, last paragraph, lines 11 to 16). Obviously, they never saw anything special about that treatment, and consequently there is no indication of confidentiality in document (3).

3.5 Accordingly, the board concludes that this teaching was performed beginning from July 1995 in the full knowledge of the patient without any obligation of confidentiality and thus was publicly available before the priority date of the patent in suit.

4. In these circumstances the arguments of the respondent cannot lead to success.

4.1 To the extent that the respondent calls for standards for a chain of evidence and arguments on the basis of the balance of probability, the board sees the argumentation of the appellant as being based on an indicative document, whereas the respondent itself tries to establish a chain of evidence and arguments to

cast doubt on a document which *prima facie* appears to be decisive. Thus, the required standards have a *priori* to be applied to the arguments of the respondent.

4.2 The respondent concludes from the age 29 mentioned at the beginning of document (3) and the following series of episodes of catheter-related bloodstream infections (CRBSIs) and line changes that the letter of authorisation dated 12 March 1996 (document (20b)) is related to the same patient mentioned in this letter as "HP" at the age of 30. Since, as reported in documents (12) and (20a), it was the first shipment of taurolidine from the respondent to the Canadian team after a long break, the respondent draws the further conclusion that there were no reserves from the last shipment, and the beginning of the taurolidine treatment of the patient reported in (3) thus could not have started before this shipment of March 1996. Disclosure of document (3) was consistent with this view on the basis of a simple update before printing.

But this chain of various indicia, put together from different documents that are not all known in their full context, together with the attempt to establish the identity of the patient through indirect conclusions, is not well-founded enough to cast doubt on the straightforward starting date of taurolidine-lock treatment of catheter-related bloodstream infections derived from the disclosure of document (3). In particular, the mere statement that there was an amendment of the text of document (3) is not sufficient to make such an event a reality.

4.3 The fact that the taurolidine-lock treatment at least at the beginning of the last twelve months ("New tunnelled subclavian" from table 1 of document (3)) was accompanied by systemic therapy with vancomycin and was maybe in parallel at any time with taurolidine as an additive to the nutritional solution (Ninewell's method) is irrelevant with respect to the clear intention of the Canadian team to interrupt the pattern of catheter-related bloodstream infections by use of the taurolidine-lock technique. The test was made using the taurolidine-lock and in full awareness of the problems of the patient with regard to repeated sepsis originating from the catheter and with the intention of fighting this problem by using this lock technique (see page 243, left column, lines 1 to 3). Addition of systemic vancomycin occasionally during this episode merely underlines that the lock-technique per se was directed to fight the sepsis originating from the catheter and not systemic sepsis.

Finally, document (3) even reports the authors as being convinced of the success of their use of antimicrobial taurolidine-lock with respect to infection being catheter-related (see page 243, right column, lines 6 to 9).

4.4 Since the respondent no longer maintains its argument that a real confidentiality agreement existed between itself as a supplier of taurolidine and the Canadian team as user, and since it merely affirms that confidentiality was inherent, only this inherency is to be assessed, in particular in relation to the decision of a technical board of appeal cited by the respondent (T 1057/92):

In the cited decision the acting doctor is held not to be an appropriate witness to state what information was public (see point 7 of the decision starting on page 14, sentence bridging pages 15 and 16 until the end of point 7). In the current case, however, it is sufficient that the patient was aware of the treatment he received, and public prior use does not depend on the doctor being a witness. In addition, in the cited decision novelty was discussed with regard to whether a trace of another compound was present or absent (see point 5 of the decision), while in the current case the straightforward use of a compound as such was crucial for assessment of novelty.

Moreover, the action in the Canadian hospital of using the taurolidine-lock was not typical of a clinical or even an experimental approach because it was dictated by the instant necessity to help a patient in a very desperate situation and thus had not been planned systematically as a scientific experiment.

- 4.5 Thus, the subject-matter of the sole request does not meet the requirements of Article 54 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chairman:

N. Maslin

U. Oswald