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D E C I S I O N
of 10 June 2002

Case Number: T 0503/99 - 3.3.2

Application Number: 93917947.9

Publication Number: 0652753

IPC: A61K 31/54

Language of the proceedings: EN

Title of invention:

Treatment of dentoalveolar infections with taurolidine and/or taurultam

Applicant:

ED. GEISTLICH SÖHNE AG FÜR CHEMISCHE INDUSTRIE

Opponent:

-

Headword:

Dentoalveolar infections/GEISTLICH

Relevant legal provisions:

EPC Art. 54(1), 56, 84, 111, 113(1), 123(2)
RPBA Art. 10
EPC R. 71a

Keyword:

"Main request: remittal and reimbursement of the appeal fee (no) - no proof of alleged procedural violations"
"First, second and third auxiliary requests: amended claims acceptable under Articles 84, 123(2) EPC"
"Novelty (yes)"
"Inventive step (no)"

Decisions cited:

-

Catchword:

-



Case Number: T 0503/99 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 10 June 2002

Appellant: ED. GEISTLICH SÖHNE AG
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Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 14 December 1998
refusing European patent application
No. 93 917 947.9 pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: U. Oswald
Members: G. F. E. Rampold
C. Rennie-Smith

Summary of Facts and Submissions

- I. European patent application No. 93 917 947.9, published under the PCT as WO 94/03 174, was refused pursuant to Article 97(1) EPC by a decision of the examining division posted on 14 December 1998. The decision was based on the appellant's (applicant's) main request, filed on 3 November 1995, its first auxiliary request, filed on 22 August 1988, and its second and third auxiliary requests, both filed during the oral proceedings before the examining division.

Claim 1 of the main request read as follows:

"Use of taurolidine and/or taurultam in the absence of antibiotics in the preparation of an orally acceptable medicament for the therapeutic treatment of the soft tissues surrounding a tooth."

Claim 1 of the first auxiliary request was worded as follows:

"Use of taurolidine and/or taurultam in the absence of antibiotics in the preparation of an orally acceptable medicament for the therapeutic treatment of dental gangrene, parodontitis or dental abscesses."

Claim 1 of the second auxiliary request read as follows:

"Use of taurolidine and/or taurultam in the absence of antibiotics in the preparation of an orally acceptable medicament for the therapeutic treatment solely of dental gangrene, parodontitis or dental abscesses."

Claim 1 of the third auxiliary request was worded as follows:

"Use of taurolidine and/or taurultam in the absence of antibiotics in the preparation of an orally acceptable medicament for the therapeutic treatment solely of parodontitis."

II. Of the documents cited in the course of the first instance examination proceedings and subsequent appeal proceedings the following are referred to in this decision:

- (1) G. H. Nentwig et al. "Erste klinische Erfahrungen mit Taurin-Feingranulat in der zahnärztlichen Chirurgie" publ. in Ed. Brückner, "Taurolin, ein neues Konzept zur antimikrobiellen Chemotherapie chirurgischer Infektionen, 1985, pp. 287-289
- (2) DE-A-2 618 666
- (3) G. H. Nentwig et al. "Zur Behandlung postchirurgischer Knocheninfektionen" publ. in Fortschr. Mund-Kiefer-Gesichts-Chirurgie, vol. 30, 1985, pp. 35-37
- (4) EP-A-0 521 225
- (5) GB-A-1 557 163
- (6) Dorland's Illustrated Medical Dictionary, 26th Edition, 1981, page 991, Entries: "Periodontitis"; "Periodontosis"

(7) "Praxis der Zahnheilkunde, Band 4, Parodontologie, 2. Auflage, Urban & Schwarzenberg Verlag, München-Wien-Baltimore" 1990, pp. 6-8 (submitted by the appellant with the statement of the grounds of appeal).

III. The stated ground for the refusal of the main request was that the reference in claim 1 to "*soft tissues surrounding a tooth*" represented an unacceptably broad generalisation from some specifically disclosed examples of such tissues in the application as filed. In its decision, the examining division held that this generalisation was, to the skilled reader, neither disclosed nor clearly implied on reading the disclosure of the claimed invention in the application as filed and concluded accordingly that claim 1 contravened Article 123(2) EPC.

Concerning the first auxiliary request, the examining division interpreted the content of citation (1) to disclose, *inter alia*, the use of taurolidine for the treatment of dental gangrene or dental abscesses in the absence of antibiotics. It concluded therefrom that the content of (1) was prejudicial to the novelty of claim 1.

As to the second auxiliary request, the examining division held that the proposed limitation of the specified therapeutic application in claim 1 to a "therapeutic treatment **solely** of dental gangrene, parodontitis or dental abscesses" was acceptable under the terms of Article 123(2) EPC and found the claim novel over the prior art citations (1) and (3). With reference to its finding that claim 1 of the first auxiliary request lacked novelty, the examining

division repeated its view that citation (1) disclosed the use of taurolidine for the treatment of dental gangrene and dental abscesses. It further concluded that the treatment of apical root resection ("Wurzelspitzenresektion") with taurolidine proposed in citation (3) necessarily implied the simultaneous treatment of dental abscesses. Based on the above interpretation of the state of the art according to (1) and (3), the examining division found that the use of taurolidine for the therapeutic treatment proposed in claim 1 was obviously derivable by the skilled person from a combination of the teachings of (1) and (3).

With regard to the third auxiliary request, the examining division relied on the disclosure of citation (6) that the infectious parodontal condition "*periodontitis*" manifested itself in an "*inflammatory reaction of the tissues surrounding a tooth (periodontium) resulting from the extension of gingival inflammation (gingivitis) in the periodontium*". It concluded therefrom that "dental gangrene" was apparently a specific form of an acute parodontal condition which was commonly known and ascribed in the medical art to the basic disease "*periodontitis*" which was a synonym for "*parodontitis*". It further stated that according to (6) "*periodontitis*" ("*parodontitis*") manifested itself also in the "*formation of periodontal pockets with pus formation*" and concluded therefrom that dental abscesses were similarly examples of infectious acute parodontal conditions covered by the broader medical term "*periodontitis*" ("*parodontitis*"). In the light of this teaching in (6) and the prior art of (1) and (3), the examining division considered the proposed use of taurolidine for the treatment of "parodontitis" in

claim 1 to be obvious to a person skilled in the art and therefore devoid of inventive step.

IV. The appellant lodged an appeal against this decision and submitted together with the statement setting out the grounds of appeal a revised main request and revised first, second, third and fourth auxiliary requests.

V. During oral proceedings, held on 10 June 2002, the appellant cancelled all earlier requests and presented, instead, its current main request and three further amended sets of claims forming its current first, second and third auxiliary requests.

The appellant's **main request** was that the decision under appeal be set aside and that the case be remitted to the examining division on account of alleged serious procedural violations and that the appeal fee be reimbursed. In the event that the main request should be refused, the appellant requested that the decision under appeal be set aside and a patent be granted on the basis of its **first, second or third auxiliary requests**.

Claim 1 in the **first auxiliary request** is worded as follows:

"Use of taurolidine and/or taurultam in the absence of antibiotics in the preparation of an orally acceptable medicament for the therapeutic treatment of dental gangrene, parodontitis marginalis and dental abscesses."

Dependent claims 2 and 3 relate to elaborations of the use according to claim 1.

Claim 1 in the **second auxiliary request** reads as follows:

"Use of taurolidine and/or taurultam in the absence of antibiotics in the preparation of an orally acceptable medicament for the therapeutic treatment of parodontitis marginalis."

Dependent claims 2 and 3 relate to elaborations of the use according to claim 1.

Claim 1 in the **third auxiliary request** is worded as follows:

"Use of taurolidine and/or taurultam in the absence of antibiotics in the preparation of an orally acceptable medicament for the therapeutic treatment of dental gangrene or dental abscesses."

Dependent claims 2 and 3 relate to elaborations of the use according to claim 1.

VI. The appellant argued, as regards its main request for remittal of the case to the examining division, that there had been two procedural violations at the oral proceedings before that division on 22 September 1998. The alleged violations were the raising for the first time at those oral proceedings of a number of matters as follows.

First, it was said that the examining division raised objections of novelty and inventive step, not previously notified to the appellant, in relation to the main claim of each of its first, second and third auxiliary requests. That claim essentially corresponded to claim 2 of the main request which had been on file

unamended since the original filing date.

Second, the appellant complained that an objection under Article 123(2) EPC was taken for the first time at the oral proceedings in relation to an amendment to claim 1 of the main request which had been made some four years before, on 26 August 1994, and on the basis of which correspondence about novelty had been conducted in the interim.

The appellant's representatives admitted, in answer to a question from the board, that they had not asked for an adjournment of the oral proceedings when these allegedly new matters were raised.

VII. As regards the patentability of the claimed use of taurolidine and/or taurultam in the claims of all current auxiliary requests, the appellant argued essentially as follows:

The alleged invention concerned the treatment of severe dental infections caused by a mixed flora of aggressive, pathogenic bacteria. Specifically, the appellant's invention related to the treatment of soft tissue infections of the mouth, namely dental gangrene, parodontitis and dental abscesses, which involved administration to the infected tissue of the methylol-transfer agents taurolidine and/or taurultam. Such infections were associated with severe inflammation of the soft tissues and remained a common cause of pain and discomfort in many patients. Inflammatory conditions of the soft tissues of the mouth were notoriously difficult to treat. In part this was due to the complex aetiology of oral infections coupled with the growing problem of bacterial resistance to

conventional antibiotics, such as tetracyclines.

Concerning novelty the appellant submitted that there was no disclosure in the prior art relating to the use of taurolidine in treating the specific soft tissue infections recited in the current claims, i.e dental gangrene, parodontitis marginalis and dental abscesses. In relation to citation (1), the examining division relied on the passage at page 287, left-hand column, line 7 and the second paragraph in the right-hand column on page 289 to suggest that (1) described the use of taurolidine in treating dental gangrene and dental abscesses. Specifically, the examining division misinterpreted the sentence starting at line 5 on page 287 of (1) which reads: "*Eintrittspforten für die bakterielle Infektion sind in der Regel der kariöse, gangränöse Zahn....*". Contrary to the suggestion of the examining division, this passage did not describe the treatment of dental gangrene. Rather, this passage referred to the gangreneous tooth as a possible mode of entry for bacteria which in turn may lead to inflammation of soft tissues or bones. There was absolutely no suggestion in any cited document that taurolidine, either with or without antibiotics, had been used in treating dental gangrene.

Also in relation to citation (1) the examining division relied on the reference to "*infizierte Zysten*" to raise an objection of lack of novelty, suggesting that these corresponded to dental abscesses. This was quite simply not the case. The authors of (1) suggested that the results obtained using taurolidine in treating alveolitis might, in future, find application in other areas of maxillofacial surgery, specifically in treating acute parodontal conditions associated with

infection of the bone tissues. "*Infected cysts*" were listed among these conditions. However, it was evident to any skilled reader that these were bone cysts, ie infected cavities within the bone which in many cases could lead to alveolitis. Contrary to the suggestion of the examining division, bone cysts neither corresponded nor overlapped with the generally accepted definition of dental abscesses.

Specifically, in relation to citation (3), the examining division made reference to the use of taurolidine in the treatment "*apikaler Paradonthopathien in Verbindung mit einer Wurzelspitzenresektion [of apical root resection]*". There was nothing in (3) which described or suggested the use of taurolidine in the treatment of a dental abscess nor indeed in treating any soft tissue infection. The foregoing observations and conclusions were clearly supported by the Statement of Professor Nenntwig, who was a co-author of citations (1) and (3). This statement was submitted as "Annex C" to the statement of the grounds of appeal.

As regards inventive step, the appellant concluded that neither (1) nor (3) taught or suggested a solution to the problem of treating severe inflammatory infections of the soft tissues of the mouth. The conditions intended to be treated in accordance with the alleged invention were quite distinct from those described in citations (1) and (3) which were concerned with the treatment of conditions associated with bacterial infection of the jaw bone and not the soft tissues. Bacteria and their toxins typically found in infected bone in the case of the severe complication of osteomyelitis of the jaw bone included gram-positive

bacteria such as *Staphylococcus aureus* and their exotoxins. Such bacteria were different from the gram-negative bacteria more commonly associated with infections of the soft tissues. Administration of an agent which was ineffective against colonised resistant bacteria present would tend to result in proliferation of these species and incomplete elimination of the infection. On this basis, it would not be the expectation of those skilled in the art that taurolidine might be effective to treat inflammation of the soft tissues of the mouth associated with special pathogenic bacteria.

The aim of the dental surgeon in treating parodontitis was the reduction of aggressive bacterial flora and their toxins. Surprisingly, the appellant had found taurolidine to be particularly effective against oral-specific, resistant gram-negative bacteria responsible for soft tissue infections. Successful adjuvant therapy of inflammatory conditions in the mouth associated with anaerobic bacterial infection using taurolidine was proven by the clinical results given in the application. Relapses had not been observed. In the light of the unknown aetiology of the flora of the mouth, the effectiveness of taurolidine against aggressive resistant parodontal germs could not have been predicted at the priority date of the alleged invention. When compared to conventional antibiotics, the superiority of taurolidine in the treatment of severe dental infections was considered surprising.

Reasons for the Decision

1. The appeal is admissible

Main request; Remittal

2. The raising of objections for the first time at oral proceedings could well amount to a substantial procedural violation if there has indeed been no prior notice of an objection, with the result that a party is taken by surprise, and if no opportunity is given for the party to consider the new objection either by way of an adjournment or, if necessary, postponement of the oral proceedings or continuation of the proceedings in writing. In such circumstances, a party might properly complain its right to be heard had been violated, in which case a board of appeal could, in the absence of special reasons, remit the case to the first instance to allow the party the fair first instance hearing it had been denied (Articles 113(1) and 111 EPC and Article 10 Rules of Procedure of the Boards of Appeal).

However, it is necessary to take all the circumstances of a particular case into account and, in the circumstances of the present case, the board holds that there were no procedural violations.

- 2.1 As regards claim 2 of the main request as filed in the original application on 29 July 1993, the appellant is incorrect in saying this had not been the subject of any specific objections based on (1) or (2) prior to the oral proceedings. In the International Preliminary Examination Report of 8 November 1994, there was a novelty objection to inter alia claims 1 to 3 based on (3) which is substantially the same as (1) and a general inventive step objection by reference to all the cited documents which included (1), (2) and (3).

In the communication of 27 June 1995 there were novelty

objections to claims 1 to 3 based on both (1) and (3) and a further inventive step objection based generally on (1), (2) and (3). In point 1 of this communication the appellant's particular attention had been drawn to the first paragraph in the left-hand column on page 287 of (1), which referred, in the opinion of the examining division, under the heading "*Einleitung und Problemstellung*" to the "*the use of taurolidine for combatting severe dental infection such as gangrene, dental abscesses, alveolitis*". Attention had also been drawn in point 1 of this communication to the reference to the condition "peridontitis" in the last seven lines on page 289 of (1).

The communication of 10 April 1996 maintained an inventive step objection to claim 2 based on (2). The Appellant filed comprehensive answers to all these communications. The communication of 11 February 1998 which accompanied the summons to oral proceedings did not repeat those particular objections but stated that the points made therein were "*in support to the objections put out in the precedent letters*" and the summons set the date of 22 August 1998 for written submissions and amendments under Rule 71a EPC.

- 2.2 In reply to that last communication the appellant's representative sent a faxed letter on 19 August 1998 enclosing an amended set of claims marked "*Auxiliary Request I*" and said to "*replace claims 1-4 currently on file*". The letter also made clear that the appellant considered this set of claims an acceptable alternative to those previously submitted and, if the examining division also found this set of claims acceptable, the oral proceedings would be unnecessary. Contrary to the appellant's hopes expressed in that letter, matters

were not resolved on the basis of that set of claims before the oral proceedings. According to the minutes of those proceedings, the appellant was asked at the outset to "formulate his request" and stated that its main request was that filed on 2 November 1995.

2.3 It is thus clear that, because of two changes of mind by the appellant, the examining division found itself one month before the oral proceedings asked in effect to treat a set of claims marked "Auxiliary Request I" as the only request and then, at the opening of the oral proceedings, found itself asked to treat the former main request as such. It is also pertinent to observe that the appellant filed two further requests (called "*Auxiliary Requests II and III*") during the oral proceedings. The examining division, which would undoubtedly have prepared for the oral proceedings on the assumption that "*Auxiliary Request I*" was the appellant's preferred (and probably only) request, must have itself been surprised at the appellant's change of position when the oral proceedings began. The appellant may in turn have felt surprised by certain of the objections taken to its requests during the oral proceedings but, if the oral proceedings were in the event less than wholly satisfactory, the file shows that the appellant, and not the examining division, was primarily responsible for that by its changes of requests. And moreover, the appellant could have asked, but did not ask, for an adjournment if it felt the objections raised at the oral proceedings such as to require time for consideration.

2.4 Accordingly, the board does not find the alleged procedural violations proved and the corresponding requests for remittal and reimbursement of the appeal

fee must be refused.

First, second and third auxiliary requests

Amendments (Article 123(2) EPC)

3. All references below to support for the present version of the claims in the originally filed documents are to the international application published under the PCT as WO 94/03 174.

3.1 Claim 1 in all three requests has been amended by explicitly excluding the use of taurolidine and/or taurultam in combination with antibiotics for the claimed therapeutic treatment.

The use of taurolidine and/or taurultam for the suggested therapeutic applications "*in the absence of antibiotics*" is clearly implied by and therefore derived from the whole disclosure as such. Thus, the description refers repeatedly in the first three paragraphs on page 2 to the risk of severe and harmful side-effects associated with the conventional treatment of dental infections using antibiotics. In the penultimate paragraph on page 3 it is expressly stated that taurolidine is effective against oral infections, but exhibits a much reduced level of side-effects. The superiority of taurolidine over the antibiotic Aureomycin® in treating dentoalveolar infections is moreover apparent from the in-vivo tests presented in the application (see especially pages 9 to 16). The aforementioned disclosures in the description are explanatory and can, in the absence of any suggestion or reference in the complete specification to the possibility of using taurolidine in the presence of

antibiotics, only mean that the use of taurolidine in the absence of antibiotics is directly and unambiguously derivable from the original disclosure. The later clarification by expressly excluding the presence of antibiotics from claim 1 was simply considered necessary to delimit more clearly the claimed subject-matter from the state of the art according to citation (4).

- 3.2 References to the use of taurolidine and/or taurultam as the active agent in medicaments for the therapeutic treatment of the particular dental infections specified in claim 1 of the auxiliary requests, ie dental gangrene, parodontitis marginalis and/or dental abscesses, may be found throughout the originally filed specification, *inter alia*, at page 4, lines 31 to 32; page 5, lines 9 to 10; page 8, lines 7 to 11; page 9, lines 24 to 27; and in claim 2. Specific reference to the treatment of paradontitis marginalis may be found at page 9, line 26.
- 3.3 Medicaments containing taurolidine or taurultam in various galenic preparations for the treatment of dental gangrene, parodontitis marginalis and/or dental abscesses are disclosed, *inter alia*, in the original description from page 9, penultimate paragraph to page 11, Table 1; in Examples 1 to 6; and in claims 4 and 5.
- 3.4 Dependent claims 2 and 3 are contained in identic form in all current auxiliary requests. Dependent claim 2 corresponds to originally filed claim 3 and dependent claim 3 results from a combination of originally filed claims 4 and 5.

- 3.5 The present version of the claims in all three auxiliary requests is therefore acceptable as being adequately supported by the disclosure in the application as filed and complying in this formal respect with Articles 84 and 123(2) EPC.

The closest state of the art

4. During the oral proceedings before the board, the appellant suggested that citation (5) represents the closest state of the art. This citation relates to the use taurolidine in the treatment of tooth and gum infections and in particular "*parodontosis*" (see especially column 1, lines 9 to 11). The appellant and its technical expert explained at the oral proceedings, and the board is satisfied that, in contrast to "*parodontitis*", "*parodontosis*" is a non-inflammatory condition of the "*periodontium*" ["*parodontium*"] and that, contrary to what is stated in (5), column 1, lines 25 to 37, parodontosis is not caused by bacterial infections. Furthermore, it is clear that citation (5) is mainly concerned with preparations for the hygiene of the mouth, including the teeth, eg tooth paste, tooth gel and mouth wash (see Examples 1 to 12) rather than with medicaments for combatting severe bacterial infections of the mouth.

- 4.1 On the other hand, citations (1) and (3) propose the use of taurolidine as an alternative treatment of serious osteomyelitis of the jaw bone. Specifically, both of these citations concern the use of taurolidine in treating alveolitis, a special form of osteomyelitis associated with bacterial infections of the jaw bone. As is described in both citations (1) and (3), alveolitis manifests itself as a severe local

inflammation of the alveolar bone, e.g. following tooth extraction.

- 4.2 The claimed subject-matter in the application concerns the treatment of severe dental infections caused by a mixed flora of aggressive, pathogenic bacteria. Specifically, the claimed invention relates to the treatment of certain well-known infections within the alveolar region of the jaw, that is to say dental gangrene (first and third auxiliary request), parodontitis marginalis (first and second auxiliary request) or dental abscesses (first and third auxiliary request).
- 4.3 In view of the observations in points 4 to 4.2 (supra), the board is convinced that citations (1) or (3) represent a closer state of the art than citation (5).

The problem and the solution

5. Starting from citations (1) or (3) as representing the closest state of the art, the problem the patent application sets out to solve is that of finding further uses for the medicaments taurolidine and taurultam in addition to those already disclosed in the state of the art. The solution to the problem relates to the use of taurolidine and taurultam in the preparation of an orally acceptable medicament for the treatment of the various dental infections specified in claims 1 to 3 of the appellant's current requests.
- 5.1 The application includes the results of clinical trials which were conducted on a representative number of patients, according to a prospective, prolective, randomized, monocentre and simple blind design, in

order to test the effectiveness of taurolidine for a number of orodental indications against therapy using 4 conventional finished antibacterials (ie Aureomycin® ointment 3%; Dontisolon® ointment-1g cont.: 5mg prednisolone, 2mg neomycin HCl, 3mg aminoquinuride 2HCl, excipients; CHKM® solution- 1ml cont.: 295mg p-chlorophenol, 767mg camphor, 18mg menthol; Chlorhexamed® dental gel 1%- 1g cont.: 10mg chlohexidine, digluconate, excipients). The results obtained in these trials demonstrate that, in the treatment of severe dentoalveolar infections, including alveolitis, dental gangrene, parodontitis marginalis and dental abscesses, all target variables (pain, swelling, secretion, pressure pain, percussion) fell more quickly under taurolidine medication than under conventional therapy (see page 9, line 5 to page 16, Table 5). Given these results and, moreover, in the absence of any evidence to the contrary, the board finds that the stated problem is indeed credibly solved by the solution now claimed.

Novelty

6. Contrary to the finding in the decision of the examining division, the board cannot recognise in the prior art available in the present proceedings either an explicit or implicit disclosure relating to the use of taurolidine or taurultam in treating the specific dental infections recited in claim 1 of any of the appellant's current auxiliary requests. As regards the actual disclosure of publications (1) and (3) which were cited by the examining division against the novelty of the claimed subject-matter in the application and their relevance to the issue of novelty in the present case, the board unhesitatingly concurs

with the appellant's submissions in writing and at the oral proceedings (see paragraph VII above). In particular the board cannot see how the skilled reader could, even on the basis of the explanations given in (6) and his general knowledge of the art, arrive at the conclusion that either (1) or (3) discloses directly and unambiguously the use of taurolidine or taurultam in the treatment of dental gangrene, parodontitis marginalis or dental abscesses. The claimed solution to the above defined problem in appellant's current first second and third auxiliary requests is accordingly found to be novel within the meaning of Article 54(1) EPC.

Inventive step

7. For the purposes of inventive step the question to be examined is whether the claimed solution would have been obvious to those skilled in the art attempting to solve the problem posed on the basis of their knowledge of the state of the art according to (1) or (3).
- 7.1 Both citations (1) or (3) contain the information that taurolidine is a widely used, non-toxic, antimicrobial chemotherapeutic agent which is highly effective against a broad spectrum of clinically relevant gram-positive **and** gram-negative germs, including all important pyrogenic cocci, the entire group of enterobacteria, mykobacteria, pseudomonas and clostridia and, moreover, 23 classes of pathogenic fungi. In the cited documents, it is explained that the methylol groups of taurolidine bind irreversibly to bacterial cell walls and membranes resulting in rapid cell death and concomitant inactivation of endo-toxins and exo-toxins. Furthermore, taurolidine possesses

marked antiadherence properties and has been demonstrated to block the attachment processes for both gram-positive and gram-negative bacteria to host cell surfaces. Given this multiple mode of action, it is said in (3) that emergence of bacterial resistance to taurolidine in microbial pathogens has so far not been observed and is also not to be expected in future (see (1), especially page 287, right-hand column, first full paragraph; (3), especially page 36, left-hand column, first full paragraph).

7.2 In view of the encouraging results reported in (1) and (3) for the use of taurolidine in dental medicine for the treatment of alveolitis (ie a special form of osteomyelitis associated with bacterial infection of the jaw bone), the authors of the cited documents suggested the application of taurolidine in other areas of maxillofacial surgery, specifically to combat other infections which have become established in the underlying jaw infrastructure, eg dentoalveolar infections, such as acute "*parodontopathies marginales*" associated with infection of the bone tissues (akute marginale Pradontopathien mit Knochenbeteiligung), "*apical parodontopathies*" associated with apical root resection (apikale Paradontopathien in Verbindung mit einer Wurzelspizenresektion) or "infected cysts" (see (1), especially page 289, right-hand column; (3), especially page 37, left-hand column).

7.3 As explained by the appellant's technical expert at the oral proceedings, about 90 percent of the various parodontal conditions covered by the generic medical term "parodontopathy marginalis" used in (1) and (3) relate to inflammatory, infectious conditions of the parodontium marginalis and are commonly known in the

medical art as "parodontitis marginalis". Parodontitis marginalis is caused by bacterial infection and encompasses both parodontitis marginalis superficialis and parodontitis marginalis profunda. As can be seen from (7)- see especially the column bridging pages 7 and 8, both these forms of parodontitis marginalis are associated with bacterial infection **of all parts of the parodontium marginalis**, including the gingiva, cementum **and** alveolar bone.

7.4 In support of an inventive step of its alleged invention, the appellant argued essentially that the bacteria and their toxins found in infected jaw bone in the case of alveolitis basically included gram-positive bacteria and their exo-toxins and that those skilled in the art would not have expected taurolidine to be similarly effective against the flora of aggressive, oral-specific, resistant and multi-resistant gram-negative bacteria with unknown aetiology responsible for the specific soft tissue infections of the mouth recited in claim 1 of the appellant's current requests.

7.5 The appellant's arguments are not convincing for several reasons. First, the state of the art clearly teaches that taurolidine is equally effective against a broad spectrum of gram-positive **and** gram-negative bacteria and their exo- and endo-toxins as well. Second, bacterial resistance to taurolidine in microbial pathogens of any kind has not yet been reported in the state of the art and no evidence to the contrary has been provided. Third, from the disclosure in the application under appeal, it is clear that documents (1) and (3) and likewise claim 1 of all three auxiliary requests are concerned with the use of taurolidine in the treatment of a similar kind of

dental infections which are all found in the underlying jaw infrastructure (parodontium), namely dentoalveolar infections, such as alveolitis, parodontitis marginalis, gangrene and dental abscesses. Fourth, the claimed use of taurolidine includes, at least in the case of parodontitis marginalis, the treatment of inflammatory conditions of both soft tissues **and** bone tissues of the mouth.

- 7.6 To summarize, in the light of the known antimicrobial properties of taurolidine, the known effectiveness of taurolidine in the treatment of alveolitis (i.e. a specific form of severe dentoalveolar infection), and moreover the suggestion in (1) and (3) of using taurolidine in the treatment of parodontopathy marginalis (including infection of soft and bone tissues of the mouth), those skilled in the art, faced with the problem to be solved, could reasonably expect that the desired result would be achieved and that taurolidine would also be similarly effective in treating other dentoalveolar infections such as parodontitis marginalis, dental gangrene and dental abscesses. In the present situation, those skilled in the art were, in the board's judgment, provided by the cited prior art with a clear pointer in the direction of the alleged invention, and it was then only necessary to confirm experimentally that the highly probable result was in fact obtained. The necessity of experimentally confirming a reasonably expected result does not render an invention unobvious. The board thus finds that none of the auxiliary requests is based on an inventive step and that the requirements of Article 56 EPC are accordingly not met.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

A. Townend

U. Oswald