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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO DIVISIÓN DE NUEVAS CREACIONES

E S. D

SUPERINDUSTRIA Y COMERCIO

Radicación: 00005195 00000003

Folios: 2

Fecha (MM): 2003-04-10 16:38:10

Trámite: 1 002 PATENTES D 1 REGISTRADO/ 538 PETICION

Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

Ref Expediente No 00-085 195

Solicitud de Patente a nombre de
NOVARTIS AG

Yo, JIMENA ESCOBAR URIBE, identificada como aparece al pie de mi firma, domiciliada en Bogotá, en la Carrera 11 A No 94-76 Of 305, obrando como apoderada de la sociedad NOVARTIS AG, domiciliada en Basilea, Suiza, solicitante de la patente de la referencia, pido a usted que se proceda a examinar si la invención, cuya patente se tramita en el expediente de la referencia, es patentable

Adjunto al presente memorial el recibo No 03 - 23,762 de abril 3, 2003, por la suma de \$335 000 oo, con lo cual queda cubierta la tasa oficial correspondiente a dicho estudio

Señor Superintendente,



JIMENA ESCOBAR URIBE

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T P 68 228

Cod 5376

JEU/ra

2388/p 106 102

SUPERMINISTERIO Y COMERCIO
Radicacion : 00085193 00000005 Folios: 2
Fecha (AMB) 2003-04-10 16 28:10
Tramite : 002 PATENTES D 1 REGISTRO/ 330 PETICION
Dependencia: 2029 DIVISION DE NUEVAS CREACIONES

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 03 - 23,762
FECHA : ABRIL 3 DE 2003

***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No PAGO	FECHA PGO	Vr PAGO
ESCOBAR URIBE ASOCIADOS	CONSIGNACION	BANCO POPULAR	050-00110-6	7034866	02/04/2003	10,934,000

***** C O N C E P T O *****

CANT. RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1 50005-01-01 SOLICITUDES	112 PTC CAP-1 EXAMEN DE PATENTE DE INVENCION	335,000
	TOTAL :	335,000 00

SON: TRESCIENTOS TREINTA Y CINCO MIL PESOS

RESPONSABLE



RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____

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**SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISIÓN DE NUEVAS CREACIONES**

2020

Bogotá, D C , 24 de enero de 2006

Apoderado Jimena Escobar Unbe

Oficio n° 1403

REFERENCIA Radicación No 0-85195
 Trámite 002
 Evento 001
 Actuación 430
 Folios

Como resultado del examen de fondo, realizado con fundamento en el artículo 45 de la decisión 486 de la Comisión de la Comunidad Andina, se le comunica

Documentos estudiados

- ◆Capítulo descriptivo folios 3 a 31,
- ◆Capítulo reivindicatono, folios 32 a 36,
- ◆1° examen de forma, folio 41,
- ◆Solicitud de la cual se reivindica prondad, folios 45 a 94, ✓
- ◆2° examen de forma folio 103,
- ◆Solicitud del examen de patentabilidad, folios 105 y 106

Objeto de la Invención

La presente solicitud cuyo título es "DERIVADOS DE PLEUROMUTILINA Y VALMUTILINA USADOS PARA LA FABRICACIÓN DE UN MEDICAMENTO PARA EL TRATAMIENTO TRANSDÉRMICO DE INFECCIONES BACTERIANAS EN HUMANOS Y ANIMALES Y COMPOSICIONES QUE LOS CONTIENEN" El objeto de la solicitud es un nuevo uso de valdemullina para la terapia en infecciones bacterianas en humanos y animales

El objeto de la invención se puede clasificar según la clasificación internacional como A61K 31/22

Reivindicaciones de uso

De acuerdo con la legislación colombiana el uso que se reclama en las

relivindicaciones 1 a 8, 10 a 12 y 14 no se considera para protección por patente, como se lee en el artículo 14 de la Decisión 486 de la Comisión de la Comunidad Andina" Los Países Miembros otorgarán patentes para las invenciones sean de **productos o procedimientos** en todos los campos de la tecnología ", AQUÍ NO se hace alusión al uso

Continuando con la última parte del Artículo 14" (Los Países Miembros otorgarán patentes para las invenciones sean de **productos o procedimientos** en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial " El hecho que se diga que el producto o el procedimiento tengan aplicación industrial no quiere decir que la aplicación industrial sea susceptible de patente

Así mismo, citando completamente el artículo 19 este reza " Se considerará que una *invención (léase producto o procedimiento)* es susceptible de aplicación industrial (*una característica de la invención*) cuando su objeto puede ser producido o utilizado en cualquier clase de industria, entendiéndose por industria la refenda a cualquier actividad productiva, incluidos los servicios " Esta diciendo que una invención, producto o procedimiento, debe servir para algo En ningún momento se dice que un uso pueda ser protegido como patente

El artículo 16 dice " Los productos o procedimientos (*o sea, los inventos, nótese que nunca se refieren a nada diferente*) ya patentados comprendidos en el estado de la técnica de conformidad con el Artículo 21 de la presente Decisión, no serán objeto de nueva patente por el simple hecho de atribuirse un uso distinto al originalmente comprendido por la patente inicial " Nunca se refieren a una protección para el uso, como erróneamente se podría interpretar Se trata de no conceder nueva patente a un invento (exclusivamente productos o procedimientos) al que se le ha encontrado nueva función, pero que se trata exactamente del mismo producto o procedimiento Es decir, sí el compuesto, aparato, etc o método ya esta dentro del estado de la técnica, el hecho que se haya descubierto una nueva aplicación para el mismo compuesto, aparato, etc o método, implica que no es merecedor de nueva patente, o que el nuevo uso le reestablezca la novedad En ningún caso se dice que se esta protegiendo el uso Simplemente se dice que el producto o procedimiento ya esta dentro del estado de la técnica y una utilización diferente no esta contemplada para permitir conceder patente al producto o al procedimiento nuevamente

Los usos o segundos usos no son patentables, de conformidad con la

sentencia del TJAC 89-AI-2000, los usos en general no son patentables

Excepciones de Patentabilidad

El artículo 20 de la Decisión 486 de la Comisión de la Comunidad Andina establece en su inciso d) que no serán patentables *"los métodos terapéuticos o quirúrgicos para el tratamiento humano o animal, así como los métodos de diagnóstico aplicados a los seres humanos o a animales"*

Las reivindicaciones 13, reclama un método para tratamiento del cuerpo humano o animal, el cual incluye la administración de un compuesto conocido del estado de la técnica en una cantidad eficaz, por lo tanto están inmersas bajo el alcance del artículo 20 de la Decisión 486

Claridad de la solicitud

En el artículo 30 de la decisión 486 de la Comisión de la Comunidad Andina se establece *"Las reivindicaciones definirán la materia que se desea proteger mediante la patente. Deben ser claras y concisas y estar enteramente sustentadas por la descripción"*

-La reivindicación no son claras, puesto que no es congruente el encabezado con el resto del texto o parte caracterizante de la reivindicación, se encabeza como una composición y el resto del texto es una mezcla de uso con método terapéutico, lo correcto es caracterizar técnicamente dicha composición como tal, sin rellenar el texto de las reivindicaciones, con notas no técnicas que no definen ningún elemento la composición

Evaluación de los requisitos de patentabilidad

El artículo 14 de la Decisión 486 de la Comunidad Andina establece que *"Los Países Miembros otorgarán patentes para las invenciones, sean de producto o de procedimiento en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial"*

En cumplimiento del artículo 14 de la Decisión 486, se procedió a evaluar los requisitos de novedad, nivel inventivo y aplicación industrial con el fin de establecer la patentabilidad de la invención reivindicada en la solicitud en estudio

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Reivindicaciones 1 a 7 se refiere a materia no patentable (folio 35), consultada la fuente de información con que cuenta este despacho se encontró los siguientes documentos que describen los compuestos y composiciones usadas en la presente solicitud, US 3 716 579, WO9921655, WO9725309, US4 675 330, WO9801127, US4 032 530, US 4 148 890, US5578585, US4428953, US4060542, EP0153277, Comité for veterinary medical products Tiamutlin simmsry report

En cumplimiento del artículo 45 de la decisión 486 de la Comisión de la Comunidad Andina, se le indica que debe dar respuesta dentro del término de sesenta días contados a partir de la fecha de la notificación de la presente comunicación. En caso de no dar respuesta al presente requerimiento, o si a pesar de la respuesta subsistieran los impedimentos para la concesión, se denegará la patente.

Notifíquese conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo 5° del título 1° de la Circular Unica n° 10 de 2001.

ALIX CARMENZA CÉSPEDES DE VERGEL

Jefe de la División de Nuevas Creaciones

09 FEB. 2003

El anterior requerimiento fue notificado por fijación en lista de fecha _____

CONCEPTO TÉCNICO No 106	EXAMINADOR TÉCNICO Código 202012
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IX. Evidence presented (evidence to follow with postal confirmation)		Enclosed = ☒ will be filed at a later date = ☐	for EPO use only
A. Publications:			Publication date
① US 3,718, 579 Particular relevance (page, column, line, fig.):			
② Committee for Veterinary Medical Products Tiamulin Summary Report (1) EMEAMRL/ST800-FINAL Particular relevance (page, column, line, fig.):			
③ WO 98/21855 Particular relevance (page, column, line, fig.):			
④ WO 97/25389 Particular relevance (page, column, line, fig.):			
⑤ US 4,879,330 Particular relevance (page, column, line, fig.):			
⑥ WO 98/01127 Particular relevance (page, column, line, fig.):			
⑦ US 4,032, 830 Particular relevance (page, column, line, fig.): For relevance Please see the Notice			
Continued on additional sheet		☐	
B. Other evidence			
Continued on additional sheet		☐	

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Notice of Opposition to EP 1 231 915 B1 Granted to Novartis AG

The Opposition period for the above identified patent expires 16 Nov 2005 and thus this Notice is filed within the relevant time frame required by Art 99(1). Instructions for the debit of the fee are contained on the attached EPO form 2300 1

Claims 1 to 6 and 8 of the patent are hereby opposed on one or more of the following grounds specified in Art 100(a) is the subject matter of the patent is not patentable with the terms of Articles 52 to 57, particularly the claims of the patent lack novelty and an inventive step. Furthermore, it will be asserted below that all the claims as granted do not meet the criteria of Art 100(b) because the patent does not disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

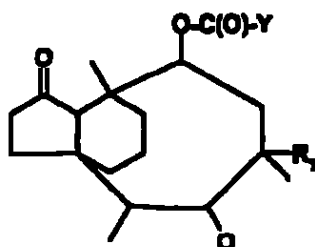
Documents Relied On.

- D1 US 3,716,579,
- D2 Committee for Veterinary Medical Products *Tumult Summary Report (1)*
The European Agency for the Evaluation of Medicinal Products,
Veterinary Medicines & Information Technology Unit
EMEA/MRL/578/99-Final August 99,
- D3 WO 99/21855
- D4 WO 97/25309,
- D5 US 4,675,330,
- D6 WO 98/01127, and
- D7 US 4,032,530

The patentee was aware of some or all of the prior art relied on in this opposition because the corresponding US case US 6,852,756, which granted 16 February 2005, was amended to overcome the disclosure of one or more of these documents

Technical Background

Claim 1 of the patent as granted relates to use of compounds of formula (I)



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wherein

R₁ represents ethyl or vinyl, andY can represent a number of moieties including -CH₂R₂ and R₂ can represent H (ie Y is -CH₃),

or a pharmaceutically acceptable salt form thereof, for the manufacture of a medicament for the transdermal treatment of bacterial infections in humans and animals.

The description page 4 paragraph 16 states.

It has now been found, surprisingly, that the compounds of the formula (I) are able to penetrate through the skin, meant here is the epidermis, without being metabolized and deactivated. It was absolutely unpredictable [emphasis added] that an antibiotic of such a complex chemical structure could pass the skin-barrier and penetrate into the tissue, and reach blood and plasma concentrations that are high enough to control successfully bacterial infections. These bacterial infections embrace systemic infections where the bacteria colonize intestine cells, tissues or organs, and non-systemic infections where the bacteria colonize a smaller or larger portion of the skin [emphasis added]. This is one of the exceptional cases where the an antibiotic can be applied to the skin instead of being applied for the treatment of systemic infections via a conventional systemic route such as orally or percutaneously. The novel use should not be confused with the conventional cutaneous use of an antibiotic for disinfecting areas of skin that are infested with the pathogen."

Paragraphs 21 & 22 go on to say

"In the present technique, the animal absorbs the compound through the skin. The compound is usually applied in a composition containing a physiologically acceptable carrier. A wide range of appropriate carriers may be employed. The composition may be a cream. A liquid composition, however, is particularly convenient to use, e.g. facilitating measuring out doses, and facilitates absorbance through the skin. The compounds of the formula (I) may be formulated for cutaneous topical administration as ointments, creams, lotions, shampoos, powders, sprays, dips, aerosols, drops, pour-ons / spot-ons or by manual methods."

These definitions of in the patent extend the usual meaning of transdermal from.

"absorption through the skin into the bloodstream" -Merriam-Webster Online

to include, what the skilled person would generally consider topical because, for example it includes *non-systemic infections where the bacteria colonize a smaller or larger portion of the skin* and simple topical formulations such as creams can be formulated for *"cutaneous topical administration"*. This clearly falls within the dictionary definition of topical

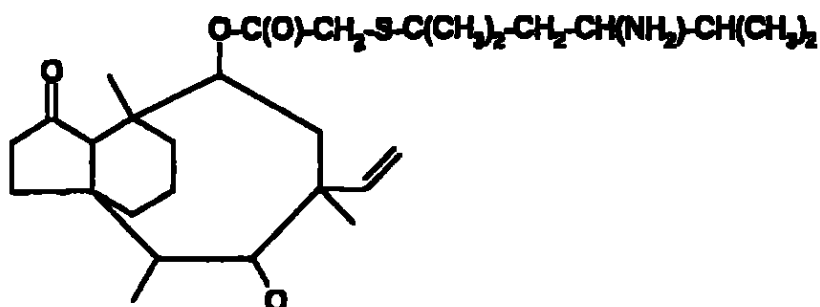
"designed for or involving local application and action"

-Merriam-Webster Online.

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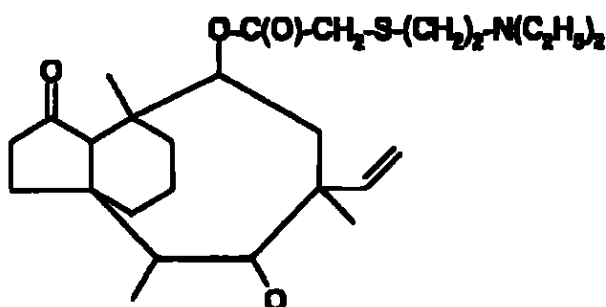
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The most preferred compounds for the said use are valnemulin, which has the following structure



and

tiemulin, which has the following structure



Novelty Article 54 EPC

D1 was published 13 February 1973 and therefore it is Art 54(2) art to the opposed patent. It discloses compounds of formula (I), of the opposed patent, wherein the substituent corresponding to R₁ is vinyl and the substituent corresponding to Y can be -CH₃ (see column 1 lines 5 to 21).

Column 4 lines 20 to 24 of D1 goes on to say

"More particularly the derivatives are active against staphylococci and streptococci. In use, the derivatives may be provided in the form of a solution or paste and applied topically to the udder of a cow. The concentration of the derivatives in the solution or paste may conveniently be between 0.0001 and 5mg/ml."

Staphylococci and streptococci are associated with mastitis, that is inflammation of the mammary gland tissue. Thus D1 teaches that compounds, of a formula that overlap with the compound of formula (I) defined in the opposed patent, can be used to treat "systemic infections where the bacteria colonize, threaten or organs", namely mastitis in the udder of cows, by application of a paste or solution to the udder i.e. truly transdermal use of the compounds

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D1 discloses all the features of the claim 1 and claim 8 and thus these claims lack novelty over this document. Furthermore, where the formulation in D1 is a solution it would arguably meet the criteria for a pour-on or spot-on formulation and thus claim 6 also lacks novelty over D1

D2 was published August 1999, before the earliest priority date of the patent and therefore this document is Art 54(2) prior art to the opposed patent.

It discloses in paragraph 16

"Tiamulin is not used in human medicine. In a patch study in humans, topical administration of a 0.05% formulation did not cause skin irritation or sensitisation."

Tiamulin is one of the preferred compounds disclosed in the opposed patent. It is submitted that this topical administration falls within the definitions of transdermal given in paragraphs 21 and 22 of the opposed patent, which are quoted above. To state it another way following the teaching of this prior art document the compound is inevitably administered transdermally because it is application of tiamulin (one of the preferred compounds according to the opposed patent) in a manner described in the opposed patent. Thus by following the teaching of D2 the skilled person is provided with the "claimed invention" of the opposed patent.

D2 discloses all the features of the claims 1, 4, 5 and 8. Thus these claims lack novelty

D3 was published 6 May 1999 before the earliest priority date of the opposed patent and thus is Art 54(2) prior art to the opposed patent.

It discloses certain compounds for use as antimicrobials.

Table 1 below includes an example comparing some of the compounds, which fall within the scope of D3 and the compounds employed in the opposed patent. Please note that "X" and the other variables are referred to as they are in the relevant document.

Table 1

Opposed Patent

R_1 = vinyl or ethyl

OH

$m = 0, 1, 2, 3, 4$ etc

Y for example = $-S(CH_2)_mX$

X = a saturated or unsaturated 5- or 6-membered heterocyclic ring which is bound to the $-S-(CH_2)_m-$ group through a carbon atom, and which contains one or more heterogroups selected from the group consisting of O, S, N or $-NR^3$ [optionally substituted]

Corresponding substituent in D3
(see page 2)

R^1 = vinyl or ethyl

R^2 = H or OH

$m = 0, 1$ or 2

$-(CH_2)_nS(CH_2)_mR^2$ ($n=0$ & $X=S$)

R^2 = a non-aromatic monocyclic or bicyclic group containing one or two basic nitrogen atoms and attached through a ring carbon atom

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It is clear the prior art compounds of D3, at least, overlap with the compounds employed in the opposed patent. The full extent of the overlap has not been defined here as it is sufficient for the purpose of supporting the opposition to simply show the patent lacks novelty

D3 goes on to state page 17 lines 10 to 15

"The compounds of the invention and compositions according to the invention may be formulated for administration by any route, for example oral, topical [emphasis added] or parenteral in the form of tablets, capsules, powders, granules, lozengers, creams, syrups, sprays or liquid preparations for example, solutions or suspensions"

More specifically on page 15 lines 25 and 26, D3 indicates

"Compounds of the present invention may be used to treat skin and soft tissue infections and acne, by topical application."

Firstly the latter falls within the definition of non-systemic infection as described in the opposed patent. Therefore, D3 discloses transdermal administration, within the meaning of the opposed patent.

It is also submitted that the disclosure of D3 implicitly discloses transdermal administration, within the meaning of the opposed patent, of the compounds therein because at least some of the compounds in this prior art document are the "same" as those employed in the opposed patent and their administration as a cream, spray or liquid etc is described. These are the very methods used to effect transdermal delivery of the compounds employed in the opposed patent and when the "same" compounds are employed (as in D3) this would inevitably result in transdermal delivery. Thus by following the teaching of the prior art document D3 the skilled person is inevitably provided with the subject matter subsequently claimed in the opposed patent.

D3 directly and unambiguously describes all the features of claims 1, 4, 6 and 8 of the opposed patent. Thus these claims lack novelty over D3

D4 was published 17 July 1997 and is Art 54(2) prior art in respect of the opposed patent. It discloses certain antimicrobial pleuromutilin compounds where the substituent, which corresponds to Y, in the claims of the opposed patent, is a cyclic group of 3 to 8 ring atoms, optionally containing one additional heteroatom selected from N, O and S, and optionally fused to a hydrocarbon ring, a heterocyclic group or an aromatic group.

R¹ in these compounds represents vinyl or ethyl. All other features of the compounds of D4 are the same as those of formula (I) in the opposed patent

D4 goes on to disclose on page 10 lines 5 to 10 that

"The compounds and compositions according to the invention may be formulated for administration by any route, for example oral, topical"

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[emphasis added] or parenteral in the form of tablets, capsules, powders, granules, lozengers, creams, syrups, or liquid preparations, for example, solutions or suspensions "

Page 10 line 33 to page 11 line 7 indicates

"Compositions according to the invention intended for topical administration may, for example, be in the form of ointments, creams, lotions and may contain appropriate conventional additives, including, for example, emollients in ointments and creams. Such topical formulations may also contain compatible conventional carriers, for example cream or ointment bases, and ethanol or oily alcohol for lotions."

Based on the same reasoning given above for D3, it is submitted that D4 discloses transdermal administration within the meaning of the opposed patent, of compounds the relevant compounds. Therefore, the claims 1 and 8 lack novelty over this document.

Disclosure of the Invention Art 83 EPC

In the situation the Opposition Division consider that one or more of the documents D1 to D4 do not render the granted claims of the opposed patent lacking in novelty, it is submitted that the patent is insufficient because it fails to teach the skilled person how to carry out the invention as required by Art 83 EPC

More particularly, the patent does not teach the skilled person how to effect transdermal delivery of the compounds across the whole scope of the granted claims. Rather it simply describes routine topical formulations of known compounds.

Relatively little guidance is given in the patent as to how to effect transdermal delivery. However paragraph 21 states

"A liquid composition, however, is particularly convenient to use and facilitates absorbance through the skin. Thus, a solution or suspension of the compound in a liquid carrier is preferred. Solutions are especially good for transmitting the compound through the skin and are therefore most preferred"

The patent also states in paragraph 15

"The novel use should not be confused with the conventional cutaneous use of an antibiotic for disinfecting areas of skin that are infested with the pathogen"

but fails to explain how this conventional use differs from the treatment of:

" non-systemic infections where the bacteria colonize a smaller or larger portion of the skin" -(paragraph 15)

by

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then the claims do not involve an inventive step as they do not provide the technical solution of transdermal delivery across the whole scope claimed.

• D5 US 4,675,330

Discloses compounds of the type employed in the opposed patent where Y represents $-S-C(CH_3)_2-CH_2-NH-C(O)-Q$ D5 column 3 lines 22 to 27 indicates:

"The compounds may be administered orally, locally [emphasis added] or parentally"

This disclosure may be sufficient to render claims 1, 2, 4 and 8 of the opposed patent lacking novelty, but to the extent that the EPO would consider that this disclosure is inadequate to be an anticipation then it certainly renders those claims lacking an inventive step given that it was known before the priority date of the patent to administer pleuromutilins transdermally (within the meaning of the opposed patent) Evidence of the fact that it was known to administer pleuromutilins transdermally is found in the documents such as D1, D3 and/or D4 above, which describe transdermal use, within the meaning of the opposed patent.

Alternatively, D5 in combination with one or more of D1, D2, D3 or D4 render claims 1 to 4 and claim 8 obvious because each of these documents describe transdermal use of a pleuromutilin compound and D5 simply describes alternative pleuromutilin compounds, which the skilled person would use transdermally as described in one more of these documents. Furthermore, a skilled person would be motivated to combine documents from the same technical field, especially given that there is no inherent incompatibility in the teaching of the same.

• D6 WO 98/01127

This document discloses pleuromutilins of the valnemulin type (one of the preferred compounds employed in the opposed patent).

Given that it was known before the earliest priority date of the opposed patent to deliver pleuromutilins transdermally, within the meaning ascribed by the opposed patent, then claims 1, 2, 3, 5 and 8 are obvious after consideration of this document.

Alternatively, D6 in combination with one or more of D1, D2, D3 or D4 render claims 1, 2, 3 5 and claim 8 obvious, because starting from D6 it would be routine to use the compounds therein in the topical/transdermal administration described in one or more of D1 to D4. Furthermore, a skilled person would be motivated to combine documents from the same technical field, especially given that there is no inherent incompatibility in the teaching of the same.

• D7 US 4,832,430

Discloses compounds of the type in the opposed patent where Y represents: $-(CH_2-Z)_r-(CH_2)_s-Q$

wherein

Z is S,

r is 1,

s is 2 to 5, and

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$Q_{12} - NR^4R^5$ and R^4 and R^5 are each C_{1-3} alkyl

Given that it was known before the earliest priority date of the opposed patent to deliver pleuromuhins transdermally, within the meaning ascribed by the opposed patent, then claims 1, 4 and 8 are obvious after consideration of this document.

Alternatively, D7 in combination with one or more of D1, D3 or D4 render claims 1, 4 and 8 obvious because starting from D7 it would be routine to use the compounds therein in the topical/transdermal administration described in one or more of D1 to D4. Furthermore, a skilled person would be motivated to combine documents from the same technical field, especially given that there is no inherent incompatibility in the teaching of the same.

In the event the Opposition Division intends to maintain the patent, including in an amended form, oral proceedings are hereby requested under Art 116 EPC.



Juha A. Florence
European Patent Attorney