

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 11-112331- -00011-0000

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Señor

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

E. S. D.

REF: Expediente No. PCT/11-112331

TÍTULO SOLICITADO: "SALES DE ADICIÓN DE TROMETAMINA CON
DERIVADOS DE ÁCIDO
AZABIFENILAMINO BENZOICO COMO
INHIBIDORES DE DHODH"

PUBLICACIÓN: Gaceta 650 del 15/08/2012, N° de publicación 1157.

SOLICITANTE: ALMIRALL S.A.

APODERADO: LUZ CLEMENCIA DE PÁEZ.

TRÁMITE: Recurso de Reposición y en subsidio el de apelación en
contra de la Resolución 60077 de octubre 17 de 2013 por
la cual se concede una patente de invención tramitada
bajo el número de expediente PCT/11-112331.

TITO NOÉ PARRA MURILLO, mayor de edad, identificado como aparece al pie de mi
firma, reconocido apoderado de la sociedad LAFRANCOL S.A.S. en el asunto de la
referencia, de manera respetuosa, y dentro de los términos de ley, presento Recurso de
Reposición y en subsidio de apelación contra la Resolución 60077 de octubre 17 de 2013
por la cual se concedió a la solicitud PCT/11-112331 el privilegio de patente de invención.

TOTAL F
15

I. PETICIÓN

Sírvase, Señor Superintendente, reponer íntegramente la Resolución 60077 de octubre 17 de 2013, por la cual se declaró infundada la oposición presentada y se otorgó el privilegio de patente solicitado en el expediente de la referencia, y en su remplazo emitir otra que, con fundamento en los argumentos expuestos en el escrito de observación y en el presente escrito, declare fundada dicha oposición y niegue el privilegio de patente mencionado, procediendo luego al definitivo archivo del expediente en cuestión.

II. ARGUMENTOS SOBRE LOS FUNDAMENTOS DE LA CONCESIÓN Y MOTIVOS DE INCONFORMIDAD

La Resolución 60077 de octubre 17 de 2013, que concede el privilegio de patente de invención solicitado para el capítulo reivindicatorio del expediente 11-112331 titulado **“Sales de adición de trometamina con derivados de ácido azabifenilaminobenzoico como inhibidores de DHODH”**, viola flagrantemente la Decisión 486 si se tiene en cuenta que existían motivos suficientes para afectar los requisitos de novedad y nivel inventivo de la solicitud en mención. Es evidente que el solicitante y la Resolución cometen un error cuando afirman que la oposición presentada por mi representada no muestra ningún tipo de argumento soportado técnicamente, ni desvirtúa la patentabilidad del objeto de estudio, declarándola infundada por cuanto, al momento de presentación del escrito de oposición se dejó en claro que para el presente caso nos encontramos frente a una combinación de compuestos, lo cual indudablemente afecta el requisito de nivel inventivo, éste mismo indispensable para acceder a cualquier beneficio patentario.

Así las cosas, me permito reiterar que la concesión de patente objeto del presente escrito se ve afectada por los documentos del estado del arte que fueron presentados inicialmente en el escrito de observación, por lo cual, basado en lo siguiente, solicito respetuosamente a ese Despacho dar análisis completo y a cabalidad sobre los siguientes documentos, los cuales sin lugar a dudas objetan la concesión en mención, toda vez que develan de manera expresa y sucinta lo que se pretende proteger en la presente solicitud.

Dicho así, me permito manifestar que agentes tales como Infliximab, Etanercept, Adalimumab, Rituximab, Tacrolimus, entre muchos otros, han sido ampliamente divulgados en el sector químico-farmacéutico, y concretamente se han develado materias muy similares, las cuales ruego a ese Despacho analizar, en los siguientes documentos:

- **WO 9216553**
- **WO 9406476**
- **US 5605690**
- **WO 9729131**
- **US 6090382**
- **WO 9411026**
- **US 5763137**
- **EP 184162**

Así como resulta imprescindible manifestar que los anteriores documentos deben ser analizados a profundidad y cabalidad para así determinar finalmente si afectan o no la novedad y nivel inventivo de la presente solicitud, toda vez que en nuestra opinión se revelan materias muy similares, también es necesario reiterar que la solicitud de la referencia pretende proteger mediante el derecho patentario objetos que no son considerados invenciones. Es claro que una invención es toda creación humana que permita transformar la materia o energía que existe en la naturaleza, para su aprovechamiento por los seres humanos y satisfacer sus necesidades concretas. De igual modo, como ya se mencionó, según los parámetros de la Decisión 486 y normas concordantes, serán patentables las invenciones que cumplan con los requisitos de novedad, nivel inventivo y aplicación industrial. No obstante, puede observarse que la solicitud en comento pretende reivindicar combinaciones, las cuales no se consideran invenciones. En este sentido, la mezcla (Combinaciones) de productos (Moléculas) conocidos y su variación, bien sea en uso, forma, dimensión o de materia, NO se consideran invenciones por cuanto no son susceptibles de aplicación industrial, nivel inventivo y novedad, luego NO pueden acceder a beneficios patentarios. Por lo tanto, se suma una circunstancia más que imposibilita definitivamente la concesión de la solicitud en mención.

Y sobre el particular, es imprescindible señalar que un efecto sinérgico nuevo no se considera inventivo como tal, dado que puede ser obvio para una persona versada en la materia, cosa que sucede en el presente caso. En palabras del Doctor Carlos Correa, *“El efecto sinérgico entre dos o más drogas se puede considerar un “descubrimiento” y no una “invención”, dado que la sinergia ocurre en el cuerpo y se descubre a través de ensayos clínicos. Asimismo, cabe destacar que, en algunos casos, las reivindicaciones de combinaciones pueden equivaler, en términos prácticos, a reivindicaciones sobre tratamientos médicos (cuya patentabilidad está excluida en la mayoría de los países), cuando sólo brindan un método para administrar una combinación de drogas conocidas.*

Asimismo, la combinación de drogas para evitar la resistencia particular a una de ellas es una práctica normal en el desarrollo farmacéutico y, por lo general, es evidente para el hombre del oficio de nivel medio” (Pautas para el examen de patentes farmacéuticas, CEIDIE, Pág. 8). En estos términos, está claro que nos encontramos frente a un tema totalmente sensible que merece toda la evaluación por cuanto las combinaciones deben considerarse excluidas de beneficios de patente.

Adicionalmente, valga señalar que las moléculas propuestas en la presente solicitud son comúnmente utilizadas en las formulaciones igualmente descritas. Dicho así, debe enfatizarse en que las formulaciones que involucran moléculas como las propuestas son totalmente conocidas y obvias por lo cual se ven afectados los requisitos de novedad y nivel inventivo. Sobre el particular, considera pertinente traer a colación menciones hechas sobre la patentabilidad de las formulaciones, las cuales podrán ilustrar más a ese Despacho:

“Como regla general, las técnicas de formulación y el conjunto de compuestos que se pueden utilizar para desarrollar productos farmacéuticos viables en sus diferentes formas, son elementos bien conocidos para una persona capacitada en la técnica... Finalmente, se debe destacar que, en términos generales, los procesos para preparar formulaciones son bien conocidos como tales y de aplicación habitual. Por lo tanto, las reivindicaciones de dichos procesos rara vez son inventivas...”¹.

Y en caso que ese Despacho decidiera insistir en el cabal cumplimiento de los requisitos exigidos para acceder al beneficio de patente, me permito allegar copia del International Search Report y el respectivo Written Opinion Of The International Searching Authority, documentos en los cuales se resalta que la presente invención no cumple con los requisitos de novedad y nivel inventivo por cuanto existen documentos citados del estado del arte que afectan de manera definitiva tales exigencias. Lo anterior deja entrever, sin lugar a equívocos, que la presente solicitud no debió ser concedida, por lo cual es procedente la revocatoria de la Resolución objeto de este escrito.

En este sentido, reitero con el debido respeto la necesidad de analizar a profundidad los requisitos de novedad y nivel inventivo para así determinar si la presente solicitud es merecedora de concesión de privilegio de patente.

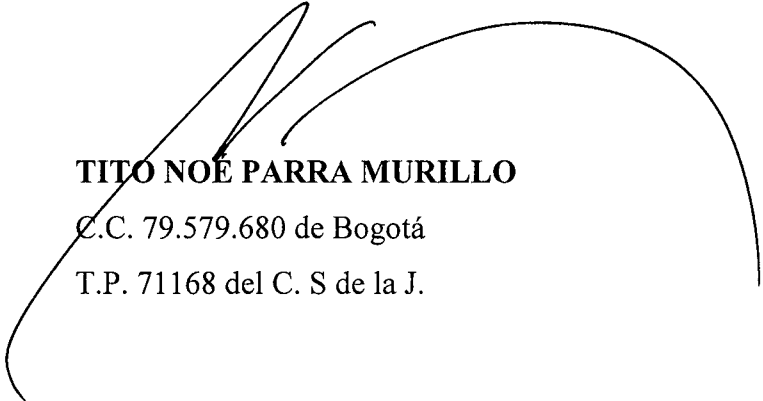
¹ Correa, Carlos. *Pautas para el examen de patentes farmacéuticas. Una perspectiva desde la Salud Pública*. Universidad de Buenos Aires. 2008. Páginas 6-7.

ANEXOS

- 1- International Search Report y el Written Opinion Of The International Searching Authority de la equivalente internacional WO 2010/102825.

En subsidio apelo.

Señor Superintendente,



TITO NOÉ PARRA MURILLO

C.C. 79.579.680 de Bogotá

T.P. 71168 del C. S de la J.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference N.110185 RCS	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/EP2010/001549	International filing date (day/month/year) 11/03/2010	(Earliest) Priority Date (day/month/year) 13/03/2009
Applicant ALMIRALL, S.A.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of:

- ☒ the international application in the language in which it was filed
☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6bis(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☐ **Unity of invention is lacking** (see Box No. III)

4. With regard to the title,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- ☒ the text is approved as submitted by the applicant
☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. _____
☐ as suggested by the applicant
☐ as selected by this Authority, because the applicant failed to suggest a figure
☐ as selected by this Authority, because this figure better characterizes the invention
b. ☒ none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2010/001549

A. CLASSIFICATION OF SUBJECT MATTER				
INV. C07D213/74	C07D239/42	A61K31/44	A61K31/506	A61P17/00
A61P19/00	A61P33/06	A61P35/00	A61P37/00	
ADD.				
According to International Patent Classification (IPC) or to both national classification and IPC				
B. FIELDS SEARCHED				
Minimum documentation searched (classification system followed by classification symbols) C07D A61K A61P				
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched				
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, EMBASE, BIOSIS, BEILSTEIN Data, CHEM ABS Data				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of the relevant passages			Relevant to claim No.
Y	WO 2009/021696 A (ALMIRALL LAB [ES]; CASTRO PALOMINO LARIA JULIO CE [ES]; TERRICABRAS BE) 19 February 2009 (2009-02-19) cited in the application page 8, lines 16-24; claims 1-31; examples 20,97,116 page 9, lines 1-4 ----- -/-			1-18
☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.				
* Special categories of cited documents :				
"A" document defining the general state of the art which is not considered to be of particular relevance				
"E" earlier document but published on or after the international filing date				
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)				
"O" document referring to an oral disclosure, use, exhibition or other means				
"P" document published prior to the international filing date but later than the priority date claimed				
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention				
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone				
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.				
"&" document member of the same patent family				
Date of the actual completion of the international search		Date of mailing of the international search report		
18 May 2010		31/05/2010		
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Sáez Díaz, R		

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2010/001549

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GU L ET AL: "Preformulation salt selection. Physical property comparisons of the tris(hydroxymethyl)aminomethane (THAM) salts of four analgesic/anti-inflammatory agents with the sodium salts and the free acids" PHARMACEUTICAL RESEARCH, KLUWER ACADEMIC PUBLISHERS, NEW YORK, NY, US, vol. 4, no. 3, 1 January 1987 (1987-01-01), pages 255-257, XP002099348 ISSN: 0724-8741 page 257	1-18
Y	US 2003/004171 A1 (HUMPHREY GUY R [US] ET AL) 2 January 2003 (2003-01-02) page 2, paragraph 13; claims 1-10	1-18
Y	STAHL P H ET AL: "Tromethamine" HANDBOOK OF PHARMACEUTICAL SALTS PROPERTIES, SELECTION AND USE, XX, XX, 1 January 2002 (2002-01-01), pages 324-325, XP002214621 page 324 - page 325	1-18

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2010/001549

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2009021696 A	19-02-2009	AR 067886 A1	28-10-2009
		AU 2008286349 A1	19-02-2009
		CA 2695475 A1	19-02-2009
		EP 2178840 A1	28-04-2010
		PE 09032009 A1	15-07-2009
		UY 31272 A1	30-01-2009
US 2003004171 A1	02-01-2003	NONE	

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference see form PCT/ISA/220		FOR FURTHER ACTION See paragraph 2 below	
International application No. PCT/EP2010/001549	International filing date (day/month/year) 11.03.2010	Priority date (day/month/year) 13.03.2009	
International Patent Classification (IPC) or both national classification and IPC INV. C07D213/74 C07D239/42 A61K31/44 A61K31/506 A61P17/00 A61P19/00 A61P33/06 A61P35/00 A61P37/00			
Applicant ALMIRALL, S.A.			

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465	Date of completion of this opinion see form PCT/ISA/210	Authorized Officer Sáez Díaz, R Telephone No. +49 89 2399-4887
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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2010/001549

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing filed or furnished:
 - a. (means)
 - ☐ on paper
 - ☐ in electronic form
 - b. (time)
 - ☐ in the international application as filed
 - ☐ together with the international application in electronic form
 - ☐ subsequently to this Authority for the purposes of search
4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

Box No. II Priority

1. ☐ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:
see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2010/001549

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>1-18</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-18</u>
Industrial applicability (IA)	Yes: Claims	<u>1-18</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

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Re Item II

Priority

- 1 The priority date is valid.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 2 The present application relates to addition salts of tromethamine with azabiphenylaminobenzoic acid derivatives as dihydroorotate dehydrogenase inhibitors for use in the treatment of autoimmune, inflammatory and infectious diseases.
- 3 Claim 18 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 39.1 (iv) / 67.1 (iv) PCT. The patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognise as patentable claims to the use of a compound in medical treatment, but may allow claims to a product, in particular substances or compositions for use in a first or further medical treatment.
- 4 Reference is made to the following documents:
- D1 WO 2009/021696
- D2 GU L ET AL: "Preformulation salt selection. Physical property comparisons of the tris(hydroxymethyl)aminomethane (THAM) salts of four analgesic/anti-inflammatory agents with the sodium salts and the free acids" PHARMACEUTICAL RESEARCH, vol. 4, 1987, pages 255-257, XP002099348
- D3 US 2003/004171 A1
- D4 STAHL P H ET AL: "Tromethamine" HANDBOOK OF PHARMACEUTICAL SALTS PROPERTIES, SELECTION AND USE, 2002, pages 324-325, XP002214621

Document D1 has been cited by the applicant in the description (Rule 5.1(a)(ii) PCT)).

- 5 No prior art document discloses tromethamine salts of formula (I). The free acid derivatives of the presently claimed tromethamine salts of formulae (II)-(IV) are found in document D1 (examples 20, 97, 116). It is noted that the presently claimed salts represent a novel selection from D1, because they are generally but not specifically disclosed therein (see claim 1 and on page 8, lines 16-24). Accordingly, the subject-matter of claims 1-18 is novel and meets the requirements of Article 33(2) PCT.

Documents D2, D3 and D4 are not relevant for the novelty assessment.

- 6 Document D1 is considered to be the closest prior art to the subject-matter of claims 1-18 and discloses azabiphenylaminobenzoic acid derivatives as dihydroorotate dehydrogenase inhibitors and their use in the treatment of autoimmune, inflammatory and infectious diseases (claims 1-31; page 8, lines 16-24; page 9, lines 1-4; examples 20, 97, 116). The problem to be solved by the present application resides therefore in the provision of alternative azabiphenylaminobenzoic acid derivatives with improved properties over those of the closest prior art (i.e. better water solubility and non hygroscopic). The solution to the present problem are tromethamine salts of azabiphenylamino-benzoic acid derivatives (see present examples). Starting from D1, the selection of tromethamine salts among others as a solution to the above-mentioned problem is obvious, since documents D2-D4 disclose that tromethamine salts of pharmaceutically active agents are the preferred ones due to their high water solubility and low hygroscopy (D2: page 257; D3: claims 1-10; page 2, paragraph 0013; D4: pages 324-325). Thus, the subject-matter of claims 1-18 does not involve an inventive step and does not meet the requirements of Article 33(3) PCT.

Re Item VIII

Certain observations on the international application

- 7 The subject-matter of the present claim 15 and 17 is not considered to be clear, since no instructions, in the form of any testable criteria, are available from the patent documents or from the common general knowledge allowing the skilled person to recognise, which conditions fall within the functional definition, e.g. any condition susceptible of being improved or prevented by the modulation of dihydroorotatedehydrogenase, and accordingly within the scope of the claim (Article 6 PCT). The reason for the necessity of this clarification is, that a claim referring to a condition to be treated, which is functionally defined, would not be limited to the treatment of said specified

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

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condition (here e.g. arthritis), but by contrast embraces an undefined number of conditions all allegedly capable of being improved or prevented by the modulation of said dehydrogenase. Under these circumstances the independent claim can only be regarded as clear if means are available to the skilled person for assessing whether or not an additional condition not expressly filed in the application but nevertheless affected by the administration of the said compounds is comprised in the scope of the claim.