

Señor

SUPERINTENDENTE DE INDUSTRIA

E.

S.

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 09-064160- -00013-0000

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Act. 412 REPOSPRESRECU Folios: 12



REF: Expediente No. PCT/09-64160

TÍTULO SOLICITADO: "NAFTIL FOSFORAMIDATOS DE NUCLEÓSIDO
COMO AGENTES ANTIVIRALES DEL VIRUS DE LA
HEPATITIS C"

PUBLICACIÓN: Gaceta 623 del 20/12/2010, N° de publicación 992.

SOLICITANTE: UNIVERSITY COLLEGE CARDIFF CONSULTANTS
LIMITED.

APODERADO: MÓNICA WOLF WASSERMAN

TRÁMITE: Recurso de Reposición y en subsidio el de apelación en
contra de la Resolución 9060 de marzo 8 de 2013 por la
cual se concede una patente de invención tramitada bajo
el número de expediente PCT/09-64160.

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 9060 de marzo 8 de 2013 por
la cual se concedió a la solicitud PCT/09-64160 el privilegio de patente de invención.

I. PETICIÓN

Sírvase, Señor Superintendente, reponer íntegramente la Resolución 9060 de marzo 8 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

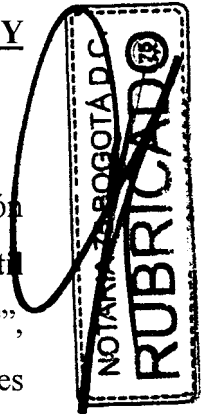
La Resolución 9060 de marzo 8 de 2013, que concede el privilegio de patente de invención solicitado para el capítulo reivindicatorio del expediente 09-64160 titulado “**Naftifosforamidatos de nucleósido como agentes antivirales del virus de la hepatitis C**”, viola flagrantemente la Decisión 486 si se 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 Abacavir, entre 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:

- EP 349242
- US 5034394

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 brindar 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.

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



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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.

ANEXOS

- 1- International Search Report y el Written Opinion Of The International Searching Authority de la equivalente internacional WO 2008/062206.

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.

~~REPUBLICA DE GUATEMALA~~

REPÚBLICA DE GUATEMALA

ALBERTO LOPEZ GARCIA

NOTARIA 75 - BOGOTÁ D.C.

Presentación Personal

18 ABR. 2013

Reconocimiento, Contenido, Firma y Huella

Este documento fue presentado

por quien se identifica como

Tito Noe Hernández Morales

cc. 7957960 del Registro Civil

quien declara que reconoce

el contenido, firma y huella

[Handwritten signature and scribbles]

Autentico y reconocido

18/4/2013

REPÚBLICA DE GUATEMALA
HILDA MARCHI AVALOS JUEZ VERIFIC
NOTARIA ENCARGADA
(75) NOTARIA 75 - BOGOTÁ D.C.

[Circular stamp: REP. GUATEMALA]

[Handwritten signature]

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
29 May 2008 (29.05.2008)

PCT

(10) International Publication Number
WO 2008/062206 A3(51) International Patent Classification:
C07H 19/20 (2006.01) A61K 31/708 (2006.01)
A61K 31/7076 (2006.01) A61P 31/14 (2006.01)(74) Agents: HOWARD, Paul, Nicholas et al.; Carpmaels &
Ransford, 43-45 Bloomsbury Square, London WC1A 2RA
(GB).(21) International Application Number:
PCT/GB2007/004480(22) International Filing Date:
23 November 2007 (23.11.2007)

(25) Filing Language: English

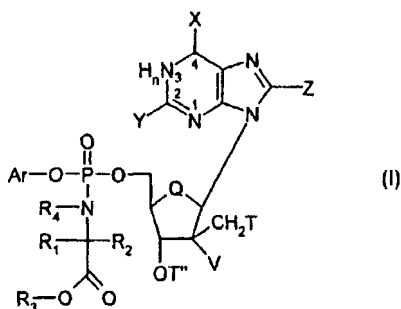
(26) Publication Language: English

(30) Priority Data:
0623493.4 24 November 2006 (24.11.2006) GB(71) Applicants (for all designated States except US): UNI-
VERSITY COLLEGE CARDIFF CONSULTANTS
LIMITED [GB/GB]; P.O. Box 497, 30-36 Newport Road,
Cardiff CF24 0DE (GB). K.U. LEUVEN RESEARCH
AND DEVELOPMENT [BE/BE]; Minderbroedersstraat
8A, B-3000 Leuven (BE).(71) Applicant (for US only): NEYTS, Johan [BE/BE]; c/o
K.U. Leuven Research and Development, Minderbroeder-
straat 8A, B-3000 Leuven (BE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): MCGUIGAN,
Christopher [GB/GB]; c/o University College Cardiff
Consultants Limited, P.O. Box 497, 30-36 Newport Road,
Cardiff CF24 0DE (GB). PERRONE, Plinio [IT/IT]; c/o
University College Cardiff Consultants Limited, P.O. Box
497, 30-36 Newport Road, Cardiff CF24 0DE (GB).(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG,
ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL,
IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK,
LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW,
MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA,
ZM, ZW.(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL,
PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report
— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments(88) Date of publication of the international search report:
10 July 2008(54) Title: NUCLEOSIDE ARYL PHOSPHORAMIDATES AND THEIR USE AS ANTI-VIRAL AGENTS FOR THE TREAT-
MENT OF HEPATITIS C VIRUS(57) Abstract: Phosphoramidate derivatives of nucleoside compounds of formula I derived from bases such as adenine and guanine have enhanced therapeutic potency, in particular, enhanced potency with respect to the prophylaxis or treatment of a viral infection such as hepatitis C virus. The glycoside moiety of the nucleoside compound is suitably substituted at the β -2' position with methyl and the phosphoramidate group, suitably comprises 1-naphthyl linked by -O- to the P atom.

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2007/004480

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07H19/20 A61K31/7076 A61K31/708 A61P31/14

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)
C07H

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, BEILSTEIN Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2006/100439 A (UNIV CARDIFF [GB]; MCGUIGAN CHRISTOPHER [GB]; MILLS KENNETH [US]; CONG) 28 September 2006 (2006-09-28) cited in the application page 26; table II claims 1,18	1-21, 23-28
A	WO 2006/012078 A (MERCK & CO INC [US]; MACCOSS MALCOLM [US]; OLSEN DAVID B [US]) 2 February 2006 (2006-02-02) cited in the application page 1, line 6 - line 11 page 22 - page 23; examples 1-4 claims 1,13	1-21, 23-28
-/--		



Further documents are listed in the continuation of Box C.



See parent 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

29. February 2008

Date of mailing of the international search report

09/05/2008

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel: (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Koch, Kristian

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2007/004480

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2006/121820 A (VALEANT RES & DEV [US]; GUNIC ESMIR [US]; CHOW SUETYING [US]; RONG FRA) 16 November 2006 (2006-11-16) page 6, line 1 - line 6 page 22, line 1 - line 2 page 23 - page 31; table 1 page 35 - page 107; table 3 claim 1	1-21, 23-28

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2007/004480

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 25 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see annex

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-21 and 23-28

Compounds of formula I, their use as anti-viral agents and a process to prepare said compounds.

2. claim: 22

Compounds of formula II.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2007/004480

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2006100439 A	28-09-2006	AU 2006226182 A1	28-09-2006
		CA 2602324 A1	28-09-2006
		EP 1866324 A1	19-12-2007
WO 2006012078 A	02-02-2006	AU 2005267421 A1	02-02-2006
		CA 2571079 A1	02-02-2006
		EP 1773355 A2	18-04-2007
		JP 2008504265 T	14-02-2008
		US 2007265222 A1	15-11-2007
WO 2006121820 A	16-11-2006	NONE	

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

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

To:

see form PCT/ISA/220

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/GB2007/004480

International filing date (day/month/year)
23.11.2007

Priority date (day/month/year)
24.11.2006

International Patent Classification (IPC, or both national classification and IPC)
INV. C07H19/20 A61K31/7076 A61K31/708 A61P31/14

Applicant
UNIVERSITY COLLEGE CARDIFF CONSULTANTS LIMITED

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 or 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 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Koch, Kristian

Telephone No. +49 89 2399-7175



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2007/004480

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 and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☐ furnished 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 and/or table relating thereto 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:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2007/004480

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

- ☐ the entire international application
- ☒ claims Nos. 22, 25 (with respect to patentability)

because:

- ☒ the said international application, or the said claims Nos. 25 (with respect to patentability) relate to the following subject matter which does not require an international search (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):
- ☒ no international search report has been established for the whole application or for said claims Nos. 22
- ☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:
- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).
- ☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See Supplemental Box for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2007/004480

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
- ☐ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is:
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-21, 23-28

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>1-21, 23-28</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-21, 23-28</u>
Industrial applicability (IA)	Yes: Claims	<u>1-21, 23-28</u>
	No: Claims	

2. Citations and explanations

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2007/004480

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.

PCT/GB2007/004480

Re Item III.

Claim 25 relates to subject-matter considered by the Authority to be covered by the provision of Rule 39.1(iv)/67.1(iv) PCT.

Re Item IV.

1. This Authority considers that there are two inventions covered by the claims indicated as follows:

Invention 1: Claims 1-21 and 23-28. Compounds of formula I, their use as anti-viral agents and a process to prepare said compounds.

Invention 2: Claim 22. Compounds of formula II.

According to Rule 13.1 PCT, the international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. This is further clarified in Rule 13.2 PCT which states that the requirement for unity of invention shall only be fulfilled when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art.

Document WO2006012078 A2, which is considered as the closest prior art, discloses nucleoside aryl phosphoramidates and their use as anti-viral agents. The special technical feature of the first invention lies in the fused aromatic ring of Ar. The technical problem underlying the first invention can be seen as the provision of further compounds for use as anti-viral agents.

Independent claim 22 describes compounds of formula II. The special technical feature of invention 2 lies in the hydroxy substituent on the phosphor atom. The description does not refer to compounds of formula II. No use of said compounds are stated neither in respect to an activity nor in the process to prepare compounds of formula I. Consequently, the

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technical problem underlying invention 2 is formulated into the provision of further organic compounds.

The solutions to the two different technical problems are not so linked to form a general inventive concept. Hence, the application lacks unity pursuant to Rule 13.1 PCT.

1.2 This written opinion only considers invention 1.

Re Item V.

2. Claim 25 relates to subject-matter considered by the Authority to be covered by the provision of Rule 39.1(v)/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 second medical treatment.

3. Reference is made to the following documents:

D1: WO2006100439 A1

D2: WO2006012078 A2

D3: WO2006121820 A1

4. Novelty.

4.1 The current application is directed towards nucleoside aryl phosphoramidates of formula I and a process to prepare them. Said compounds and their pharmaceutical compositions are active as anti-viral agents and are used to treat hepatitis C virus (HCV).

4.2 The documents D1, D2 and D3 disclose nucleoside aryl phosphoramidate and their use for the treatment of cancer (D1) and viral infections (D2 and D3). The current application differs from D1 due to the CH₂T substituent at the beta-2' position in the glycoside moiety of the nucleoside. There is no overlap between the claimed scope of

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claim 1 and D2/D3 since the Ar group which comprises two or more fused aromatic rings for the former and phenyl for D2/D3. Since the claimed nucleoside aryl phosphoramidates appears to be novel, the process to prepare these compounds, their use and pharmaceutical compositions are also novel per se. Thus, the subject-matter of claims 1-21 and 23-28 appears to be novel and meets the requirements of Article 33(2) PCT.

5. Inventive step

5.1 The documents D2 and D3 may be considered as the closest prior art since D2 and D3 disclose nucleoside aryl phosphoramidates and their use as anti-viral agents. The technical feature distinguishing the current application from D2 and D3 is the Ar group which comprises two or more fused aromatic rings. The current application contains empirical data showing an increased HCV activity over the structurally closest prior art. Thus, the technical problem to be solved is to provide improved compounds for the treatment of HCV. Given the structural differences vis-à-vis the prior art those compounds which can be reasonably considered to solve the technical problem can be considered to be inventive.

5.2 The technical problem can however, only be accepted as having been solved, if it is credible that substantially all claimed compounds possess this improved activity. It is noted that the exemplified compounds illustrate only the part of the claimed scope where Ar is a fused bicyclic compound, i.e. 1-naphtyl. For Ar containing more than two fused aromatic ring or for heteroaromatic fused ring systems no examples are provided. It is evident that a small structural change for the Ar part of formula I results in significant change in HCV activity. Therefore, it is inherently unlikely that all of the claimed compounds, or substantially all of them, will possess the promised activity.

5.3 Claim 28 relates to a process for the preparation of compounds of formula I. The patentability of said process dependent on the patentability of the claimed compounds of formula I.

5.4 Thus, the subject-matter of claims 1-21 and 23-28 appears not to involve an inventive step and fails to meet the requirements of Article 33(3) PCT.

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Re Item VIII.

6. Claims 1, 23 and 24 contain preferred embodiments. Said preferred embodiments should as such become part of separate dependent claims.

6.1 There is an unacceptable discrepancy between the claims and the description since the description (see pages 10-11) makes it clear that the terms "alkyl", "alkenyl" and "alkynyl" comprise cyclic hydrocarbon radicals. The skilled person would not have been aware of this from a reading of the claims since the skilled person would assume that standard IUPAC nomenclature was being used. In the current case, however, the Applicant has used non-standard nomenclature. The intended scope of the claims cannot be understood without referring to the description which contravenes (Rule 6.2 (a) PCT). The claims and description should be fully harmonised so that their scope is the same and so that the claims are fully clear in their own right.

6.2 The term "prodrugs" in claim 1 is a functional definition which attempts to define a chemical compound in terms of a result to be achieved. This is not allowable. The precise scope of the term is not ascertainable and it should be deleted. "Prodrugs" is a functional definition without a specific technical guidance for the selection of the suitable derivatives in the description and without proven general knowledge to show which derivatives are suitable prodrugs. This would require an equally unquantifiable and thus unreasonable amount of experimentation, imposing a severe and undue burden on all those wishing to ascertain the scope of the claim, which is not in compliance with the clarity requirement of Article 6 PCT.

6.3 The current application contains independent product claims 1 and 21. Claim 21 appears to contain all the technical features of claim 1 (Rule 6.4(a) and (b)) and should therefore be re-drafted as dependent claim.