

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 10275-0150-00304	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2019/054681	International filing date (<i>day/month/year</i>) 4 October 2019 (04-10-2019)	(Earliest) Priority Date (<i>day/month/year</i>) 5 October 2018 (05-10-2018)
Applicant VERTEX PHARMACEUTICALS INCORPORATED		

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 6 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 43.6**bis**(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, 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/US2019/054681

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61P1/16 A61P11/00 C07D471/14 C07D487/04 C07D487/14
 C07D519/00 A61K31/5377 A61K31/4985 A61K31/496 A61K31/4162
 A61K31/4439 A61K31/427 A61K31/4178 A61K31/4196 A61K31/437

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

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 practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RAGHAO S. MALI ET AL: "USEFUL SYNTHESSES OF PYRANO- AND PYRIDOINDOLES", ORGANIC PREPARATIONS AND PROCEDURES INTERNATIONAL: THE NEW JOURNAL FOR ORGANIC SYNTHESIS, vol. 26, no. 5, 1 October 1994 (1994-10-01), pages 573-577, XP055673302, US ISSN: 0030-4948, DOI: 10.1080/00304949409458060 compound 6 on pages 574 and 575 ----- -/-	1,7,14, 21



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 application or patent 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

10 March 2020

Date of mailing of the international search report

30/03/2020

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

Hanisch, Inken

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SOUMITRA MAITY ET AL: "A Visible-Light-Mediated Oxidative C?N Bond Formation/Aromatization Cascade: Photocatalytic Preparation of N-Arylindoles", ANGEWANDTE CHEMIE, INTERNATIONAL EDITION, vol. 51, no. 38, 17 September 2012 (2012-09-17), pages 9562-9566, XP055673234, DE ISSN: 1433-7851, DOI: 10.1002/anie.201205137 compound 6i, scheme 2 -----	1,3,4, 14,21
X	HUI JIANG ET AL: "Multiple Roles of the Pyrimidyl Group in the Rhodium-Catalyzed Regioselective Synthesis and Functionalization of Indole-3-carboxylic Acid Esters", ADVANCED SYNTHESIS & CATALYSIS, vol. 358, no. 2, 21 January 2016 (2016-01-21), pages 188-194, XP055673213, DE ISSN: 1615-4150, DOI: 10.1002/adsc.201500769 compound 3ra, table 2 -----	1,2,7, 14,21
X	XIA SONG ET AL: "Regioselective Synthesis of 2-Alkenylindoles and 2-Alkenylindole-3-carboxylates through the Cascade Reactions of N -Nitrosoanilines with Propargyl Alcohols", JOURNAL OF ORGANIC CHEMISTRY, vol. 83, no. 15, 3 August 2018 (2018-08-03), pages 8509-8521, XP055673186, US ISSN: 0022-3263, DOI: 10.1021/acs.joc.8b01098 compound 5p, table 3 -----	3,7,16, 21
X	MARIA LUISA SACCARELLO ET AL: "A New Synthesis of 1-Alkyl-3-aminoindoles", SYNTHESIS, vol. 1979, no. 09, 1 January 1979 (1979-01-01), pages 727-729, XP055674059, STUTTGART, DE. ISSN: 0039-7881, DOI: 10.1055/s-1979-28816 compound 7e ----- -/--	1,14,21

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2019/054681

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FORBES I T ET AL: "SYNTHESIS, BIOLOGICAL ACITIVITY, AND MOLECULAR MODELING STUDIES OF SELECTIVE 5-HT2C/2B RECEPTOR ANTAGONISTS", JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, US, vol. 39, no. 25, 1 January 1996 (1996-01-01), pages 4966-4977, XP002061494, ISSN: 0022-2623, DOI: 10.1021/JM960571V compound 32, scheme 5, page 4975 -----	1,7,10, 14,21
X	KAMAT A G ET AL: "SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF FUROINDOLE DERIVATIVES", INDIAN JOURNAL OF CHEMISTRY, JODHPUR, IN, vol. 33B, 1 January 1994 (1994-01-01), pages 255-259, XP000909708, compounds 9a-9c, scheme 2, table 1, page 259, page 256 last paragraph and page 258 first paragraph -----	1,3-7, 14,21
X	GADAGINAMATH GURU S ET AL: "Chemoselective reaction of 3,6-diacetylindole towards hydroxylamine:Synthesis and antimicrobial activity of novel", REVUE ROUMAINE DE CHIMIE, EDITURA ACADEMIEI ROMANE, RO, vol. 45, 1 January 2000 (2000-01-01), pages 929-933, XP009519202, ISSN: 0035-3930 compounds 6a-6c; scheme 1; table 2; page 933 -----	1,3-7, 14,21
X	PUTTAVVA METI ET AL: "Regioselective synthesis of dipyrrolopyrazine (DPP) derivatives via metal free and metal catalyzed amination and investigation of their optical and thermal properties", RSC ADVANCES, vol. 7, no. 29, 1 January 2017 (2017-01-01), pages 18120-18131, XP055673199, ISSN: 2046-2069, DOI: 10.1039/C7RA01795B compound 6g, scheme 1, table 2 ----- -/--	1,7,10, 14,21,43

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2019/054681

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DUNDAPPA S DONAWADE \ AV RAGHU & GURU S GADAGINAMATH*: "Synthesis and antimicrobial activity of novel linearly fused 5-substituted- 7-acetyl-2,6-dimethyloxazolo[4,5-j]indoles", INDIAN JOURNAL OF CHEMISTRY, SECTION B, COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH (C S I R), DE, vol. 46B, 1 April 2007 (2007-04-01), pages 690-693, XP009519193, ISSN: 0376-4699 compounds 5a-5d, scheme 1, table 1, page 691 and 692	1,3-7, 14,21
A	----- WO 2011/056222 A1 (UNIV PITTSBURGH [US]; PAK STEPHEN C [US] ET AL.) 12 May 2011 (2011-05-12) the whole document, in particular claims 1, 2, 5 etc., table 5, compound HA-100 with rn 1197334-04-5 -----	1-52

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2019/054681

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011056222	A1	12-05-2011	NONE

Information on Search Strategy - Pilot phase (see OJ 2015, A86)

The type of information contained in this sheet may change during the pilot for improving the usefulness of this new service.

Application Number

PCT/US2019/054681

TITLE: MODULATORS OF ALPHA-1 ANTITRYPSIN

APPLICANT: VERTEX PHARMACEUTICALS INCORPORATED

IPC CLASSIFICATION: A61P1/16, A61P11/00, C07D471/14, C07D487/04, C07D487/14, C07D519/00, A61K31/5377, A61K31/4985, A61K31/496, A61K31/4162, A61K31/4439, A61K31/427, A61K31/4178, A61K31/4196, A61K31/437

EXAMINER: Hanisch, Inken

CONSULTED DATABASES: REAXYS, WPI, NPL

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

CPC:

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:

heterocyclic compounds containing a ortho-fused tricyclic core whereby one of the two five-membered outer rings is a pyrrol ring; alpha-1 antitrypsin modulators, AAT augmentation, AAT replacement therapy, treatment of the genetic disorder alpha-1 antitrypsin deficiency, AATD, (SERPINA1, A1AT, PI, PI1, PR02275)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
see form PCT/ISA/220

PCT

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/US2019/054681	International filing date (day/month/year) 04.10.2019	Priority date (day/month/year) 05.10.2018
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International Patent Classification (IPC) or both national classification and IPC
INV. A61P1/16 A61P11/00 C07D471/14 C07D487/04 C07D487/14 C07D519/00 A61K31/5377 A61K31/4985
A61K31/496 A61K31/4162 A61K31/4439 A61K31/427 A61K31/4178 A61K31/4196 A61K31/437

Applicant
VERTEX PHARMACEUTICALS INCORPORATED

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.

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 Hanisch, Inken Telephone No. +49 89 2399-0
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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:
 - a. ☐ forming part of the international application as filed:
 - ☐ in the form of an Annex C/ST.25 text file.
 - ☐ on paper or in the form of an image file.
 - b. ☐ furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
 - ☐ in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
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 forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

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>8, 9, 11-13, 15, 17-20, 22-42, 44-52</u>
	No: Claims	<u>1-7, 10, 14, 16, 21, 43</u>
Inventive step (IS)	Yes: Claims	<u>8, 9, 11-13, 15, 17-20, 22-42, 44-52</u>
	No: Claims	<u>1-7, 10, 14, 16, 21, 43</u>
Industrial applicability (IA)	Yes: Claims	<u>1-52</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

Re Item V.

Reference is made to the following documents:

- D1 RAGHAO S. MALI ET AL: "USEFUL SYNTHESSES OF PYRANO- AND PYRIDOINDOLES",
ORGANIC PREPARATIONS AND PROCEDURES INTERNATIONAL: THE NEW JOURNAL FOR ORGANIC SYNTHESIS,
vol. 26, no. 5, 1 October 1994 (1994-10-01), pages 573-577,
XP055673302, ISSN: 0030-4948, DOI: 10.1080/00304949409458060
- D2 SOUMITRA MAITY ET AL: "A Visible-Light-Mediated Oxidative C?N Bond Formation/Aromatization Cascade: Photocatalytic Preparation of N-Arylindoles",
ANGEWANDTE CHEMIE, INTERNATIONAL EDITION,
vol. 51, no. 38, 17 September 2012 (2012-09-17), pages 9562-9566,
XP055673234, ISSN: 1433-7851, DOI: 10.1002/anie.201205137
- D3 HUI JIANG ET AL: "Multiple Roles of the Pyrimidyl Group in the Rhodium-Catalyzed Regioselective Synthesis and Functionalization of Indole-3-carboxylic Acid Esters",
ADVANCED SYNTHESIS & CATALYSIS,
vol. 358, no. 2, 21 January 2016 (2016-01-21), pages 188-194,
XP055673213, ISSN: 1615-4150, DOI: 10.1002/adsc.201500769
- D4 XIA SONG ET AL: "Regioselective Synthesis of 2-Alkenylindoles and 2-Alkenylindole-3-carboxylates through the Cascade Reactions of N - Nitrosoanilines with Propargyl Alcohols",
JOURNAL OF ORGANIC CHEMISTRY,
vol. 83, no. 15, 3 August 2018 (2018-08-03), pages 8509-8521,
XP055673186, ISSN: 0022-3263, DOI: 10.1021/acs.joc.8b01098
- D5 MARIA LUISA SACCARELLO ET AL: "A New Synthesis of 1-Alkyl-3-aminoindoles",
SYNTHESIS, vol. 1979, no. 09, 1 January 1979 (1979-01-01), pages 727-729, XP055674059, STUTTGART, ISSN: 0039-7881, DOI: 10.1055/s-1979-28816
- D6 FORBES I T ET AL: "SYNTHESIS, BIOLOGICAL ACITIVITY, AND MOLECULAR MODELING STUDIES OF SELECTIVE 5-HT_{2C/2B} RECEPTOR ANTAGONISTS",

JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, vol. 39, no. 25, 1 January 1996 (1996-01-01), pages 4966-4977, XP002061494, ISSN: 0022-2623, DOI: 10.1021/JM960571V

- D7 KAMAT A G ET AL: "SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF FUROINDOLE DERIVATIVES", INDIAN JOURNAL OF CHEMISTRY, JODHPUR, IN, vol. 33B, 1 January 1994 (1994-01-01), pages 255-259, XP000909708,
- D8 GADAGINAMATH GURU S ET AL: "Chemoselective reaction of 3,6-diacetylindole towards hydroxylamine: Synthesis and antimicrobial activity of novel", REVUE ROUMAINE DE CHIMIE, EDITURA ACADEMIEI ROMANE, RO, vol. 45, 1 January 2000 (2000-01-01), pages 929-933, XP009519202, ISSN: 0035-3930
- D9 PUTTAVVA METI ET AL: "Regioselective synthesis of dipyrrolopyrazine (DPP) derivatives via metal free and metal catalyzed amination and investigation of their optical and thermal properties", RSC ADVANCES, vol. 7, no. 29, 1 January 2017 (2017-01-01), pages 18120-18131, XP055673199, ISSN: 2046-2069, DOI: 10.1039/C7RA01795B
- D10 DUNDAPPA S DONAWADE \ AV RAGHU & GURU S GADAGINAMATH*: "Synthesis and antimicrobial activity of novel linearly fused 5-substituted- 7-acetyl-2,6- dimethyloxazolo[4,5-j]indoles", INDIAN JOURNAL OF CHEMISTRY, SECTION B, COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH (C S I R), DE, vol. 46B, 1 April 2007 (2007-04-01), pages 690-693, XP009519193, ISSN: 0376-4699
- D11 WO 2011/056222 A1 (UNIV PITTSBURGH [US]; PAK STEPHEN C [US] ET AL.) 12 May 2011 (2011-05-12)

It is noted that the scope of current claims 1, 14 and 16 is so broad that D1-D10 only are an arbitrary selection of novelty-destroying documents found.

Claims 38-42 relate 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.

Novelty

The compounds of current claims 1, 14 and 16 do not comply with the requirements of Article 33(2) PCT as at least D1-D10 disclose compounds falling within the currently claimed scope (see citations given in the international search report). The compounds claimed in current claim 13 as well as compounds S3, S6 and 32 (claims 18-20) including their claimed solid forms and their pharmaceutically acceptable salts and solvates (claims 22-37), however, are novel. Moreover, the compounds of current claims 1, 14 and 16 have not been disclosed for the currently claimed uses of treating alpha-1 antitrypsin deficiency or modulating alpha-1 antitrypsin activity so that current claims 38-42 are novel, too.

Inventive Step

E.g. D11 is considered to be the closest prior art as it discloses with HA-100 a compound which potentially is useful for the treatment of alpha-1 antitrypsin deficiency which contains the current tricyclic core structure. The current compounds differ from the compound of D11 in current substituent R¹ not being hydrogen and in current substituent R³ not being an amide group. No special technical effect has been shown to be due to this structural difference so that the current compounds are considered to solve the problem of providing further compounds which modulate alpha-1 antitrypsin activity.

In the light of D11 the skilled person had no incentive to chose the current solution of current claim 1, 14 or 16 when looking for a solution to the given problem. As a consequence, an inventive step in the sense of Article 33(3) PCT may be acknowledged for those current compounds which actually solve the given problem. In this respect it is noted that the currently claimed scope in particular in view of the fused ring containing Z¹⁻³ is much broader than the tested compounds (see current table 8).

Re Item VIII.

The requirements of Article 6 PCT are not completely fulfilled yet:

- In claims 1 (viii), 14 (ix) and 16 (viii), a proviso is present relating to cases where Z^1 , Z^2 and/or Z^3 are carbon or nitrogen which apparently restricts the meanings of substituent R^3 . Are the additional meanings of R^3 given in the definition (vi) (or (vii) in case of claim 14) intended to define further possible substituents on sulphur of a fused five-membered ring wherein all of Z^{1-3} are either oxygen or sulphur?
- The dependencies in the claims are not clear yet. E.g. the compounds of current claim 13 should be made dependent upon current independent claims 1, 14 and 16, as appropriate. Moreover, current claims 18-20 apparently should refer back to claims 1 and 14, current claims 22, 26, 28, 32-35, 44 and 47 to claim 20, claim 25 to claim 24, claim 30 to claims 24 or 29, claim 37 to claims 32-35, claim 49 to claim 18 and claim 51 to claim 19, as appropriate.
- The scope of current claims 22, 23, 25, 26, 28, 30, 33 and 35 is not clearly defined, respectively, due to substantially similar (claim 23) or as the crystal forms A-C (claims 22, 25, 26, 28, 30) or compound 32 (claims 33, 35) are not defined in the said claims despite them being drafted as independent claims.
- It is noted that current claim 41 is defined by the modulation (without any indication of which way of two diverging ways of modulation) of alpha-1 antitrypsin activity without an indication of what kind of diseases are affected thereby.
- In current paragraph [0071] inconsistencies exist leading to a doubt as to the intended scope of the term "alkyl" which does not correspond to the general understanding of the term. Should the term rather be replaced by the term "aliphatic" in the claims? In case unusual definitions of terms used in the claims are intended to apply the said definitions must be clearly derivable from reading the claims alone (see also e.g. cycloalkyl according to [0072] or alkoxy according to [0078]).