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**Datasheet for the decision  
of 12 August 2009**

**Case Number:** T 1898/06 - 3.3.01

**Application Number:** 99960668.4

**Publication Number:** 1147104

**IPC:** C07D 401/12

**Language of the proceedings:** EN

**Title of invention:**

Aromatic heterocyclic compounds as antiinflammatory agents

**Applicant:**

Boehringer Ingelheim Pharmaceuticals Inc.

**Opponent:**

-

**Headword:**

Urea derivatives/BOEHRINGER

**Relevant legal provisions:**

EPC Art. 84

**Relevant legal provisions (EPC 1973):**

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**Keyword:**

"Main Request and Auxiliary Requests 1-5: Clarity of the claims (no): The term "pharmaceutically acceptable derivatives thereof" renders the claims unclear"

"Auxiliary Request 6: Meets the requirements of the EPC"

**Decisions cited:**

T 0988/02

**Catchword:**

-



Case Number: T 1898/09 - 3.3.01

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.01  
of 12 August 2009

**Appellant:** Boehringer Ingelheim Pharmaceuticals Inc.  
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**Representative:** Kläs, Heinz-Gerd  
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**Decision under appeal:** Decision of the Examining Division of the  
European Patent Office posted 28 July 2006  
refusing European application No. 99960668.4  
pursuant to Article 97(1) EPC.

**Composition of the Board:**

**Chairman:** P. Ranguis  
**Members:** C. M. Radke  
I. Beckedorf

## Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division to refuse European patent application no. 99 960 668.4.

II. The following documents were cited during the examination proceedings:

- (D1) WO-A-98/52 558
- (D2) EP-A-0 692 483
- (D3) US-A-5 162 360
- (D4) WO-A-99/32 111
- (D5) WO-A-99/32 110
- (D6) WO-A-99/32 106
- (D7) WO-A-99/32 455.

III. The examination division considered the subject-matter of the claims to be novel, to satisfy the requirements of Article 123(2) EPC and the priority to be valid, so that documents (D4) to (D7) did not form part of the state of the art under Article 54(2) EPC. Document (D1) was considered to be the closest prior art.

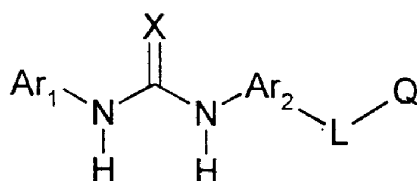
The comparative tests filed with the letters dated 10 April 2003 and 21 September 2004 failed to show a surprising effect over the whole breadth of the claims. So, the subject-matter claimed was a non-purposeful selection from the compounds generically disclosed in document (D1) and did not involve an inventive step.

IV. The claims on file are  
Claims 1-19 of the **Main Request**,  
claims 1-17 of the **First Auxiliary Request**,

claims 1-18 of the **Second Auxiliary Request**,  
claims 1-18 of the **Third Auxiliary Request**, and  
claims 1-18 of the **Fourth Auxiliary Request**,  
all enclosed with the statement setting out the grounds  
for appeal dated 24 November 2006;  
claims 1-17 of the **Fifth Auxiliary Request** filed with  
the telefax of 5 June 2009, received at the EPO at  
18.26 hrs;  
claims 1-17 of the **Sixth Auxiliary Request** filed with  
the telefax of 5 June 2009, received at the EPO at  
19.02 hrs.

(a) The relevant parts of claim 1 of the Main Request  
read as follows:

"1. A Compound of the formula (I):



wherein

Ar<sub>1</sub> is a heterocyclic group selected from the group  
consisting of pyrrole, pyrrolidine, pyrazole,  
imidazole, oxazole, thiazole, furan and thiophene;  
and wherein Ar<sub>1</sub> may be substituted by one or more  
R<sub>1</sub>, R<sub>2</sub> or R<sub>3</sub>;

Ar<sub>2</sub> is: naphthyl, tetrahydronaphthyl, indanyl or  
indenyl each being optionally substituted with one  
to three R<sub>2</sub> groups;

L is a C<sub>1-10</sub> saturated or unsaturated branched or unbranched carbon chain;  
wherein one or more methylene groups are optionally independently replaced by O, N or S;  
and  
wherein said linking group is optionally substituted with 0-2 oxo groups and one or more C<sub>1-4</sub> branched or unbranched alkyl which may be substituted by one or more halogen atoms;

Q is selected from the group consisting of:  
a) phenyl, naphthyl, pyridine, pyrimidine, pyridazine, imidazole, benzimidazole, furan, thiophene, pyran, naphthyridine, oxazo[4,5-*b*]pyridine and imidazo[4,5-*b*]pyridine, which are optionally substituted with one to three groups selected from the group consisting of halogen, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, hydroxy, mono-or di-(C<sub>1-3</sub> alkyl)amino, C<sub>1-6</sub> alkyl-S(O)<sub>m</sub> and phenylamino wherein the phenyl ring is optionally substituted with one to two groups consisting of halogen, C<sub>1-6</sub> alkyl and C<sub>1-6</sub> alkoxy;  
b) tetrahydropyran, tetrahydrofuran, 1,3-dioxolanone, 1,3-dioxanone, 1,4-dioxane, morpholine, thiomorpholine, thiomorpholine sulfoxide, thiomorpholine sulfone, piperidine, piperidinone, tetrahydropyrimidone, cyclohexanone, cyclohexanol, pentamethylene sulfide, pentamethylene sulfoxide, pentamethylene sulfone, tetramethylene sulfide, tetramethylene sulfoxide and tetramethylene sulfone which are optionally substituted with one to three groups selected from the group consisting of C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy,

hydroxy, mono- or di-(C<sub>1-3</sub> alkyl)amino-C<sub>1-3</sub> alkyl, phenylamino-C<sub>1-3</sub> alkyl and C<sub>1-3</sub> alkoxy-C<sub>1-3</sub> alkyl;  
c) C<sub>1-6</sub> alkoxy, secondary or tertiary amine wherein the amino nitrogen is covalently bonded to groups selected from the group consisting of C<sub>1-3</sub> alkyl and C<sub>1-5</sub> alkoxyalkyl and phenyl, wherein the phenyl ring is optionally substituted with one to two groups selected from the group consisting of halogen, C<sub>1-6</sub> alkoxy, hydroxy or mono- or di-(C<sub>1-3</sub> alkyl) amino, C<sub>1-6</sub> alkyl-S(O)<sub>r</sub>, phenyl-S(O)<sub>t</sub>, wherein the phenyl ring is optionally substituted with one to two groups selected from the group consisting of halogen, C<sub>1-6</sub> alkoxy, hydroxy or mono- or di-(C<sub>1-3</sub> alkyl) amino;

R<sub>1</sub> is selected from ... ;

R<sub>2</sub> is selected from ....;

R<sub>3</sub> is selected from ...

or R<sub>1</sub> and R<sub>2</sub> taken together may optionally form a fused phenyl or pyridinyl ring,

...

m = 0, 1, 2;

r = 0, 1, 2;

t = 0, 1, 2;

X = O or S and

physiologically acceptable acids or salts thereof."

- (b) Claim 19 of the Main Request, claim 17 of the First and Fifth Auxiliary Requests and claim 18 of the Second to Fourth Auxiliary Requests read as follows:

"A pharmaceutical composition comprising a compound according to claim 1 or the pharmaceutically acceptable derivatives thereof."

- (c) The claims 1 of the auxiliary requests differ from that of the Main Request in that
- the definition of the group L has been restricted in claim 1 of the First Auxiliary Request;
  - that thiophen, thiophen and furan, and thiophen, furan and pyrrole where deleted as definitions of the heterocyclic group Ar<sub>1</sub> in the Second, Third and Fourth Auxiliary Requests, respectively;
  - that the groups Ar<sub>1</sub> and Ar<sub>2</sub> have been defined as follows in claim 1 of the Fifth and Sixth Auxiliary Requests:  
"Ar<sub>1</sub> is pyrazole, wherein Ar<sub>1</sub> may be substituted by one or more R<sub>1</sub>, R<sub>2</sub> or R<sub>3</sub>;  
Ar<sub>2</sub> is: naphthyl optionally substituted with one to three R<sub>2</sub> groups;", and
  - that in the last line of claim 1 of the Sixth Auxiliary Request the words "acids or" have been deleted in the expression

"physiologically acceptable acids or salts thereof".

(d) Claim 17 of the Sixth Auxiliary Request only differs from claim 19 of the Main Request in that the expression "or the pharmaceutically acceptable derivatives thereof" has been deleted.

V. The Board summarised its preliminary and non-binding opinion in a communication annexed to the summons to oral proceedings. There it considered the expressions "physiologically acceptable acids ... thereof" and "the pharmaceutically acceptable derivatives thereof" in the claims to be vague and to render their subject-matter unclear.

VI. As to the clarity of the claims the Appellant argued that pharmaceutically acceptable salts with acids were exemplified in the application. The skilled person would readily be able to identify physiologically acceptable acids. Hence, it considered the term "physiologically acceptable acids ... thereof" to be clear.

It was evident from the application that the term "pharmaceutically acceptable derivatives thereof" meant pharmaceutically acceptable acids, salts, esters, prodrugs or metabolites. Therefore, this term was also clear.

The Appellant considered document (D1) to be the closest prior art. The problem to be solved was to provide small molecule inhibitors of cytokine production with improved efficacy. This problem was



solved. The compounds disclosed in document (D1) differed from the ones claimed in the present invention in the substructure Ar<sub>2</sub>-L-Q. Document (D1) gave no guidance to modify the compounds disclosed therein to yield the compounds presently claimed. Therefore, the subject-matter of the claims involved an inventive step.

- VII. By a telefax sent on 5 June 2009 received at the EPO at 18:26 hrs the Appellant announced that it would not attend the oral proceedings and requested a decision on the basis of the written submissions.

The Appellant requested in the written proceedings that the decision under appeal be set aside and that a patent be granted on the basis of the set of claims re-filed as Main Request with letter dated 24 November 2006 or, alternatively, on the basis of one of the sets of claims filed as First to Fourth Auxiliary Requests with letter dated 24 November 2006 or filed as Fifth Auxiliary Request with letter dated 5 June 2009 (received at the EPO at 18:26 hrs) or filed as Sixth Auxiliary Request with letter dated 5 June 2009 (received at the EPO at 19:02 hrs) (see point IV above).

- VIII. Oral proceedings were held on 12 August 2009 in the absence of the Appellant (see Rule 115(2) EPC). At the end of the oral proceedings, the decision of the Board was announced.

## Reasons for the Decision

1. The appeal is admissible.

### *Main Request and the First to Fifth Auxiliary Requests*

2. Clarity of the claims

- 2.1 In the communication annexed to the summons the Board deemed the expression "or the pharmaceutically acceptable derivatives thereof" to be vague and to render the subject-matter of claim 19 of the Main Request and the respective claims of the First to Fourth Auxiliary Request unclear (See point 2.2 of the communication).

Claim 17 of the Fifth Auxiliary Request which has been filed after the issue of said communication is identical with claim 19 of the Main Request. Hence, this objection also applies to this claim.

- 2.2 "According to Article 84 EPC, the claims shall define the matter for which protection is sought (first sentence) and for this purpose they shall, inter alia, be clear and supported by the description (second sentence). This implies that the claims be clear in themselves when being read with the normal skills, but not including knowledge derived from the description of the patent application." (decision T 988/02 of 30 October 2003, point 3.3.1 of the reasons).

Therefore, the Appellant's argument that it was clear from the description of the application what was to be

understood as pharmaceutically acceptable derivatives, cannot support clarity of the claims.

2.3 The expression "or the pharmaceutically acceptable derivatives thereof" adds to the compounds as defined in claim 1 those which are "derived" from said compounds. There is, however, no clear definition to which extent the compounds according to claim 1 may be modified while still being regarded as derivatives. This has the effect that the person skilled in the art cannot decide clearly which compounds are to be covered by the claims and which are not.

2.4 For this reason, the subject-matter of claim 19 of the Main Request, claim 18 of the Second to Fourth Auxiliary Requests and claim 17 of the First and Fifth Auxiliary Request is not clear, contrary to the requirements of Article 84 EPC.

Therefore, these requests are rejected.

2.5 The expression "physiologically acceptable acids ... thereof" in claims 1 of the Main Request and the First to Fifth Auxiliary Requests renders the claim unclear. The compounds of the formula depicted in said claims are not defined as being easily converted into acids (e.g. as esters or amides). Hence, it is unclear what is to be regarded as an acid of such a compound. The Appellant's argument seems to imply that "salts thereof with physiologically acceptable acids" were meant, contrary to the wording of the claims.

There is no need to give more detailed reasons as the Main Request and the First to Fifth Auxiliary Requests

are rejected for the reasons given under point 2.3 above, (see point V and the first paragraph under point VI above).

*Sixth Auxiliary Request*

3. Clarity of the claims

In the claims of the Sixth Auxiliary Request, the expressions "the pharmaceutically acceptable derivatives thereof" and "physiologically acceptable acids ... thereof" have been deleted. Hence, the objections listed under point 2 above do not apply to these claims. The Board is satisfied that these claims are clear.

4. Article 123(2) EPC

Claim 1 is based on claims 1, 3 and 5 as originally filed; claims 2 to 10 are based on original claims 4 and 6 to 13, respectively; claim 11 is equivalent to original claim 12 restricted to the first compound mentioned therein; claims 12 to 17 are based on original claims 14 and 17 to 21, respectively.

The amended claims thus meet the requirements under Article 123(2) EPC.

5. Novelty

None of the documents (D1) to (D7) discloses a compound of formula (I) as depicted in present claim 1 where the group Ar<sub>1</sub> is an optionally substituted pyrazole radical and the group Ar<sub>2</sub> is an optionally substituted naphthyl radical. Therefore, the subject-matter of the present claims is novel.

6. Priority

The Board is satisfied that the priority is valid for all the claims of the Sixth Auxiliary Request.

Therefore, documents (D4) to (D7) only form part of the state of the art under Article 54(3) EPC and are not to be considered when assessing inventive step.

7. Inventive Step

7.1 The closest prior art

The closest state of the art is normally a prior art document disclosing subject-matter with the same objectives as the claimed invention and having the most relevant technical features in common.

The present application deals with diaryl(thio)ureas which inhibit the production of cytokines involved in inflammatory processes (see page 1, lines 7-16).

Document (D1) also deals with the treatment of cytokine mediated diseases by means of diarylurea compounds

inhibiting the production of cytokines (see page 6, line 26 to page 7, line 2, and claim 1).

Document (D3) deals with aryl-heteroaryl-ureas and their use in the inhibition of the enzyme acyl-coenzyme A-cholesteryl acyltransferase, i.e. seek to lower the cholesterol level in blood in order to treat hypercholesterolemia and atherosclerosis, namely disorders not based on inflammatory processes (see column 1, lines 6-15).

Therefore, document (D3) does not have the same objectives as the present application, whereas document (D1) does.

Hence, document (D1) represents the closest prior art.

## 7.2 The problem to be solved

One of the problems addressed in the application as originally filed is the provision of "novel compounds which inhibit the release of inflammatory cytokines ..." (see page 10, lines 1-3). The comparative tests filed with the letters dated 21 September 2004 and 10 April 2003 show that this problem was indeed solved. Whether or not a more ambitious problem was solved need not be discussed in view of the outcome of this decision.

## 7.3 The solution

In order to modify the compounds disclosed in (D1) to yield the ones claimed in claim 1 of the Sixth

Auxiliary Request, the person skilled in the art had to replace in the formula I on page 8 of document (D1)

- (a) the radical B (defined to be a substituted thienyl, furanyl or pyrrolyl group) by a pyrazolyl group;
- (b) the optional substituent of the radical A (the only examples of which do not fall under the definition of the group -L-Q as defined in present claim 1) by a mandatory group -L-Q; and
- (c) had to select the naphthyl group from the C<sub>6-12</sub>-aryl and C<sub>5-12</sub>-heteroaryl groups A (as is disclosed on page 9, line 16 of document (D1)).

Document (D1) does not give the person skilled in the art an indication that compounds thus amended would still be cytokine inhibitors. The person skilled in the art would not have consulted document (D3) as it deals with a completely different problem (see the fourth paragraph under point 7.1 above). Document (D2) could not have directed the person skilled in the art to the compounds presently claimed as the compounds disclosed there may neither have a naphthyl nor a pyrazolyl group directly bonded to different nitrogen atoms of the urea group (see claims 1 and 2; compare claim 1 of the Sixth Auxiliary Request).

For this reason, claim 1 of the Sixth Auxiliary Request involves an inventive step. The same applies to the remaining claims of this request, namely to claims 2-11 (which are dependent from claim 1), to claims 12 to 15 (relating to the use of these compounds), claim 16 (relating to a process for making the compounds) and to

claim 17 (relating to pharmaceutical compositions containing these compounds).

8. Consequently, the claims of the Sixth Auxiliary Request meet the requirements of the EPC.

## **Order**

### **For these reasons it is decided that:**

1. The decision under appeal is set aside.
2. The case is remitted to the department of first instance with the order to grant a patent with the following claims and a description to be adapted:

claims 1 to 17 filed as Sixth Auxiliary Request with letter dated 5 June 2009 (received at the EPO at 19:02 hrs).

The Registrar:

The Chairman:

M. Schalow

P. Ranguis