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Datasheet for the decision of 24 April 2007

Case Number: T 0223/05 - 3.3.01

Application Number: 97920213.2

Publication Number: 0892789

IPC: C07D 239/94

Language of the proceedings: EN

Title of invention:
Irreversible inhibitors of tyrosine kinases

Patent Proprietor:
Warner-Lambert Company LLC

Opponent:
Wyeth

Headword:
Tyrosine kinase inhibitors/WARNER-LAMBERT

Relevant legal provisions:
EPC Art. 52(1), 54, 56, 64, 69, 84, 111(1), 123(2)(3)
EPC R. 71(2)

Keyword:
"Main request: Novelty (no) - Article 69 EPC not applicable for distinguishing the claimed subject-matter from the prior art"
"Auxiliary request I: Amendments - supported by the application as filed (no)"
"Auxiliary request II: Inventive step (yes) - non obvious solution"

Decisions cited:
G 0009/91, G 0001/99, T 0416/87, T 0270/90, T 0740/96, T 1208/97, T 0881/01, T 0671/03

Catchword:
1. Article 69 EPC and its Protocol on interpretation do not provide a basis for excluding what is literally covered by the terms of a claim (see point 3.5 of the reasons).

2. In the context of an appeal by Appellant-Opponent from an Opposition Division decision maintaining the patent in amended form, the Board of Appeal only has to consider the appeal as regards claims upon which the Appellant-Opponent has advanced arguments and those claims that are dependent, either wholly or partially, on these claims and has to apply the provision of Article 114(1) EPC in a restricted manner (see points 2.1 and 2.2 of the reasons).

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0223/05 - 3.3.01

D E C I S I O N
of the Technical Board of Appeal 3.3.01
of 24 April 2007

Appellant: (Opponent)
Wyeth
Five Giralda Farms
Madison, NJ 07940 (US)

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Taplow
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Berkshire SL6 0PH (GB)

Respondent: (Patent Proprietor)
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Representative:
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Kraus & Weisert
Patent- und Rechtsanwälte
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Decision under appeal:
Interlocutory decision of the Opposition Division of the European Patent Office posted 23 December 2004 concerning maintenance of European patent No. 0892789 in amended form.

Composition of the Board:

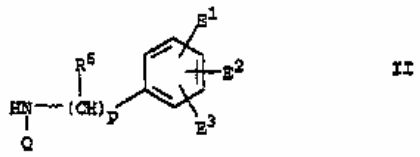
Chairman: A. Nuss
Members: P. Ranguis
D. S. Rogers

Summary of Facts and Submissions

I. The Appellant (Opponent) lodged an appeal against the interlocutory decision of the Opposition Division maintaining the European patent 0 892 789 in amended form pursuant to Article 102(3) EPC.

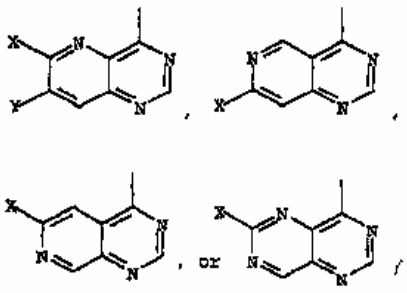
II. The set of claims maintained by the Opposition Division contains seventy claims. In particular, independent Claim 18 identical to Claim 18 as granted reads as follows:

"18. A compound having the formula II

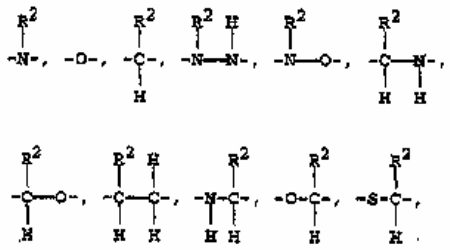


II

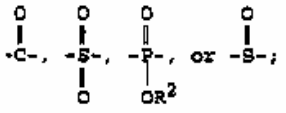
wherein Q is



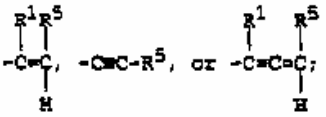
p is 0 or 1
X is -D-E-F and Y is -SR^4, -OR^4, -NHR^5 or hydrogen, or X is -SR^4, -OR^4, -NHR^5 or hydrogen, and Y is -D-E-F;
D is



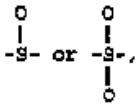
or absent;
E is



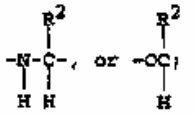
F is



provided that when E is



D is not



R^1 is hydrogen, halogen, or C_1-C_8 alkyl;
R^2, R^3, and R^4 are independently hydrogen, C_1-C_8 alkyl, -$(CH_2)_n$-N-piperidinyl, -$(CH_2)_n$-N-piperazinyl, -$(CH_2)_n$-N_1-piperazinyl[N_4-(C_1-C_8)alkyl], -$(CH_2)_n$-N-pyrrolidyl, -$(CH_2)_n$-pyridinyl, -$(CH_2)_n$-N-imidazoyl, -$(CH_2)_n$-imidazoyl, -$(CH_2)_n$-N-morpholino, -$(CH_2)_n$-N-thiomorpholino, -$(CH_2)_n$-N-hexahydroazepine or substituted C_1-C_8 alkyl, wherein the substituents are selected from -OH, -NH_2, or

A and B are independently hydrogen, C_1-C_8 alkyl, -$(CH_2)_n$OH, -$(CH_2)_n$-N-piperidinyl, -$(CH_2)_n$-N-piperazinyl -$(CH_2)_n$-N_1-piperazinyl[N_4-(C_1-C_8)alkyl], -$(CH_2)_n$-N-pyrrolidyl, -$(CH_2)_n$-N-pyridyl, -$(CH_2)_n$-imidazoyl or -$(CH_2)_n$-N-imidazoyl;
E^1, E^2, and E^3 are independently halogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_1-C_8 alkoxy, C_3-C_8 cycloalkoxy, nitro, C_1-C_8 perfluoroalkyl, hydroxy, C_1-C_8 acyloxy, -NH_2, -NH(C_1-C_8 alkyl), -N(C_1-C_8 alkyl)$_2$, -NH(C_3-C_8 cycloalkyl), -N(C_3-C_8 cycloalkyl)$_2$, hydroxymethyl, C_1-C_8 acyl, cyano, azido, C_1-C_8 thioalkyl, C_1-C_8 sulfinylalkyl, C_1-C_8 sulfonylalkyl, C_3-C_8 thiocycloalkyl, C_3-C_8 sulfinylcycloalkyl, C_3-C_8 sulfonylcycloalkyl, mercapto, C_1-C_8 alkoxycarbonyl, C_3-C_8 cycloalkoxycarbonyl, C_2-C_4 alkenyl, C_4-C_8 cycloalkenyl, or C_2-C_4 alkynyl; and
R^5 is hydrogen, halogen, C_1-C_8-perfluoroalkyl, 1,1-difluoro(C_1-C_8)alkyl, C_1-C_8 alkyl, -$(CH_2)_n$-N-piperidinyl,

-$(CH_2)_n$-piperazinyl, -$(CH_2)_n$-piperazinyl[N_4-(C_1-C_8)alkyl], -$(CH_2)_n$-N-pyrrolidyl, -$(CH_2)_n$-pyridinyl, -$(CH_2)_n$-N-imidazoyl, -$(CH_2)_n$-N-morpholino, -$(CH_2)_n$-N-thiomorpholino,

-CH=CH-(C_1-C_8)alkyl, -$(CH_2)_n$-N-hexahydroazapine, -$(CH_2)_nNH_2$, -$(CH_2)_nNH(C_1$-C_8 alkyl), -$(CH_2)_nN(C_1$-C_8 alkyl)$_2$, -1-oxo(C_1-C_8)alkyl, carboxy, (C_1-C_8)alkyloxycarbonyl, N-(C_1-C_8)alkylcarbamoyl, phenyl or substituted phenyl, wherein the substituted phenyl can have from one to three substituents independently selected from Z^1, Z^2, Z^3 or a heteroaryl group consisting of a monocyclic aromatic ring containing one or more nitrogen, oxygen, sulfur or phosphorus atoms and each C_1-C_8 alkyl group can be substituted with -OH, -NH_2 or -NAB, where A and B are as defined above, R^6 is hydrogen or C_1-C_8 alkyl; and

n is 1 to 4, p is 0 or 1, and the pharmaceutically acceptable salts, thereof".

III. Notice of opposition had been filed by the Appellant requesting revocation of the patent as granted in its entirety on the ground of lack of novelty and of inventive step in view of the following documents:

(1) US 60/011128 (Priority document of EP-A-787 722), prior art under Article 54(3) and (4) EPC,
(2) EP-A-635 498
(3) WO95/19774

IV. The Opposition Division held, in particular, that the wording of Claim 18 was silent as to the values of X, when Y was not present. In view of this lack of information, the skilled reader would have referred to the content of the description in order to clarify the value of X when Y was absent. It turned out from the description of the patent that all the claimed compounds had a Michael acceptor side-chain. Hence, the skilled reader would have corrected this lack of information in Claim 18 by the content of the description and would have concluded that in the absence of Y, X had to be a Michael acceptor side-chain. For this reason the subject-matter of Claim 18 was novel over document (3).

Furthermore, starting from document (3) as the closest state of the art, the technical problem to be solved could be seen in the provision of alternative compounds having irreversible tyrosine kinase inhibitory properties. In the absence of evidence that the technical problem was not solved within the whole scope of the claimed subject-matter, the onus of proof lying on the Opponent, the Opponent's allegation was not substantiated. Document (3) did not point the person

skilled in the art in the direction of the claimed compounds as a solution to the technical problem to be solved so that said compounds involved an inventive step.

V. In its statement of grounds of appeal, the Appellant disputed that Claim 18 was silent for the values of X, when Y was not present. From a proper understanding of Claim 18 it was clear that in this case X could take any one of the five meanings listed, namely -D-E-F-, -SR^4, -OR^4, -NHR^3 or hydrogen. It followed that the claimed compounds when Q corresponded to the second and third heterocycle moieties were anticipated by document (3) when X meant -OR^4, -NHR^3.

Regarding inventive step, the Appellant contended that, in view of document (3) as the closest state of the art, the technical problem to be solved could be seen in the provision of alternative compounds having irreversible tyrosine kinase inhibitory properties. However, no data had been provided to show a single compound encompassed by Claim 18 to be an irreversible tyrosine kinase inhibitor, far less to establish the activity across the scope of the claim. Indeed, Claim 18 covered tri-substituted phenyl compounds, i.e. in which E^1, E^2, E^3 may be anything but hydrogen. In view of the lack of data to show even a single compound of Claim 18 to be an irreversible tyrosine kinase inhibitor the burden of proof remained with the Proprietor of the patent.

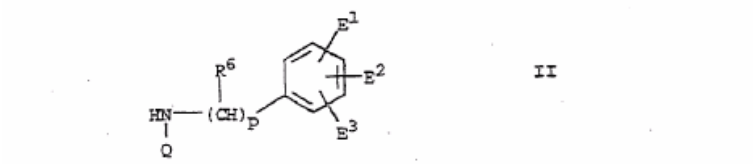
VI. At the oral proceedings before the Board, the Respondent (Proprietor of the patent) submitted two auxiliary requests.

Auxiliary request I contains seventy one claims. Compared to Claim 18 as maintained (see point II above), independent Claim 19 differs in that Q is a pyrido[4,3-d]pyrimidine, pyrido[3,4-d]pyrimidine or pyrimido[5,4-d]pyrimidine moiety and X means -D-E-F- (Q is pyrido[3,2-d]pyrimidine was deleted).

Auxiliary request II contains sixty four claims. Independent Claim 18 differs from Claim 18 as maintained (see point II above) in that Q is a pyrido[3,2-d]pyrimidine moiety (the other meanings of Q are deleted). The connotation p is 0 or 1, last line, is deleted as redundant.

Independent Claim 22 reads as follows:

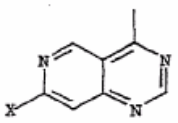
"22. A compound having the formula II



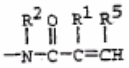
II

wherein

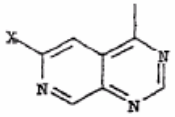
(A) Q is



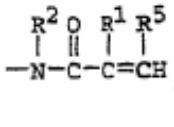
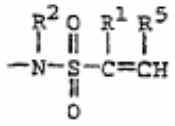
and X is



(B) or Q is



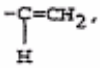
and X is


or


and wherein
p is 0 or 1

R^1 is hydrogen, halogen, or C_1-C_6 alkyl;
R^2 is hydrogen, C_1-C_8 alkyl, -$(CH_2)_n$-N-piperidinyl, -$(CH_2)_n$-N-piperazinyl, -$(CH_2)_n$-N_1-piperazinyl[N_4-(C_1-C_6)alkyl], -$(CH_2)_n$-N-pyrrolidyl, -$(CH_2)_n$-pyridinyl, -$(CH_2)_n$-N-imidazoyl, -$(CH_2)_n$-imidazoyl, -$(CH_2)_n$-N-morpholino, -$(CH_2)_n$-N-thiomorpholino, - $(CH_2)_n$-N-hexahydroazepine or substituted C_1-C_6 alkyl, wherein the substituents are selected from -OH, -NH_2, or

A and B are independently hydrogen, C_1-C_8 alkyl, -$(CH_2)_n$OH, -$(CH_2)_n$-N-piperidinyl, - $(CH_2)_n$-N-piperazinyl - $(CH_2)_n$-N_1-piperazinyl[N_4-(C_1-C_6)alkyl], -$(CH_2)_n$-N-pyrrolidyl, -$(CH_2)_n$-N-pyridyl, -$(CH_2)_n$-imidazoyl or -$(CH_2)_n$-N-imidazoyl;
E^1, E^2, and E^3 are independently halogen, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_1-C_6 alkoxy, C_3-C_8 cycloalkoxy, nitro, C_1-C_6 perfluoroalkyl, hydroxy, C_1-C_6 acyloxy, -NH_2, -NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$_2$, -NH(C_3-C_8 cycloalkyl), -N(C_3-C_8 cycloalkyl)$_2$, hydroxymethyl, C_1-C_6 acyl, cyano, azido, C_1-C_6 thioalkyl, C_1-C_6 sulfinylalkyl, C_1-C_6 sulfonylalkyl, C_3-C_8 thiocycloalkyl, C_3-C_8 sulfinylcycloalkyl, C_3-C_8 sulfonylcycloalkyl, mercapto, C_1-C_6 alkoxycarbonyl, C_3-C_8 cycloalkoxycarbonyl, C_2-C_4 alkenyl, C_4-C_8 cycloalkenyl, or C_2-C_4 alkynyl; and
R^3 is hydrogen, halogen, C_1-C_6-perfluoroalkyl, 1,1-difluoro(C_1-C_6)alkyl, C_1-C_6 alkyl, -$(CH_2)_n$-N-piperidinyl, -$(CH_2)_n$-piperazinyl, - $(CH_2)_n$-piperazinyl[N_4-(C_1-C_6)alkyl], -$(CH_2)_n$-N-pyrrolidyl, -$(CH_2)_n$-pyridinyl, - $(CH_2)_n$-N-imidazoyl, -$(CH_2)_n$-N-morpholino, -$(CH_2)_n$-N-thiomorpholino,



-CH=CH-(C_1-C_6)alkyl, - $(CH_2)_n$-N-hexahydroazepine, - $(CH_2)_nNH_2$,-$(CH_2)_n$NH(C_1-C_6 alkyl), -$(CH_2)_n$N(C_1-C_6 alkyl)$_2$, -1-oxo(C_1-C_6)alkyl, carboxy, (C_1-C_6)alkyloxycarbonyl, N-(C_1-C_6)alkylcarbamoyl, phenyl or substituted phenyl, wherein the substituted phenyl can have from one to three substituents independently selected from E^1, E^2, E^3 or a heteroaryl group consisting of a monocyclic aromatic ring containing one or more nitrogen, oxygen, sulfur or phosphorus atoms and each C_1-C_6 alkyl group can be substituted with -OH, -NH_2 or -NAB, where A and B are as defined above, R^6 is hydrogen or C_1-C_6 alkyl; and

n is 1 to 4 and the pharmaceutically acceptable salts, thereof."

VII. Oral proceedings took place on 24 April 2007. The Board was informed by a letter received on 12 March 2007 that the Appellant would not be represented at these oral proceedings. The oral proceedings were thus held in the absence of the duly summoned Appellant in accordance with Rule 71(2) EPC.

VIII. The Respondent submitted in writing and at the oral proceedings the following arguments:

The grounds of appeal only contained arguments directed against maintained Claims 18 to 25, 66 and 69. No substantiated objections were raised to Claims 1 to 17, 26 to 65, 67, 68, and 70.

The Opposition Division was correct that Claim 18 as maintained was silent regarding the meaning of X when Y was absent. In such circumstances, Claim 18 had to be interpreted by reference to the description in accordance with Article 69 EPC and its protocol of interpretation. From the description, the person skilled in the art would have understood that X in the absence of Y was a Michael acceptor. Claim 18 was, therefore, novel over Document (3).

Regarding Claim 19 of auxiliary request I, support for the amendments could be found in the description and Claim 18 as filed.

Regarding Claims 18 and 22 of auxiliary request II, starting from document (3) as the closest state of the art, the technical problem to be solved was indeed to be seen in the provision of irreversible inhibitors of tyrosine kinases. The mere allegation of the Appellant that Claim 18 comprised compounds which did not work could not be considered a convincing argument since it was not properly substantiated. The Appellant disregarded in that respect that in opposition proceedings, the burden of proof that the claimed subject-matter did not solve the technical problem remained with the Opponent.

The claimed solution was, furthermore, not obvious in view of the prior art cited, in particular document (3), since the person skilled in the art could not derive therefrom any pointer to compounds as defined in Claim 18. The same conclusion applied to claim 22.

IX. The Appellant requested in writing that the decision under appeal be set aside and the patent be revoked.

The Respondent requested that the appeal be dismissed and that the patent be maintained; or that the decision under appeal be set aside and that the patent be maintained on the basis of:

(1) Claims 1-71 of auxiliary request I dated 24 April 2007

(2) Claims 1-64 of auxiliary request II dated 24 April 2007.

X. 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

2. Scope of the appeal

2.1 The Appellant requested that the decision under appeal be set aside and the patent be revoked in its entirety. However, as submitted by the Respondent, the Appellant

only submitted arguments that granted Claims 18 to 25, 66 and 69 as maintained by the Opposition Division did not satisfy the requirements of the EPC. The Appellant did not submit any arguments regarding the other claims and did not attend the oral proceedings.

2.2 The question therefore arises whether the Board has to examine *ex officio* the other claims of the patent, against which the Appellant has not put forward any arguments.

Article 114(1) EPC provides that the EPO should examine the facts of its own motion; it shall not be restricted in this examination to the facts, evidence and arguments provided by the parties and the relief sought.

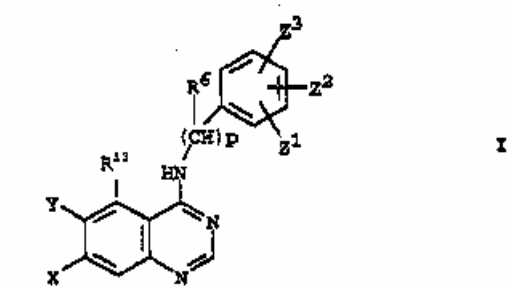
The scope of Article 114(1) EPC in the context of an appeal from an Opposition Division decision has been considered by the Enlarged Board of Appeal in G 9/91 (OJ EPO 1993, 408) where at point 18 it is stated that:

"In contrast to the merely administrative character of the opposition procedure the appeal procedure is to be considered as a judicial procedure, as explained by the Enlarged Board in its recently issued decisions in cases G 7/91 and G 8/91...Such procedure is by its very nature less investigative than an administrative procedure. Although Article 114(1) EPC formally covers also the appeal procedure, it is therefore justified to apply this provision generally in a more restrictive manner in such procedure than in opposition procedure...".

Thus, in this case the Board only has to consider the appeal as regards those claims upon which the Appellant has advanced arguments. This appeal thus concerns the compatibility with the EPC of Claims 18 to 25, 66 and 69, and those claims that are dependent, either wholly or partially on these claims (see G 9/91, loc.cit. point 11).

2.3 The patent in suit claims three different types of compounds and their respective therapeutic applications, either in the form of a pharmaceutical composition, or in the form of the use of a compound for the preparation of a pharmaceutical composition for treating a disease.

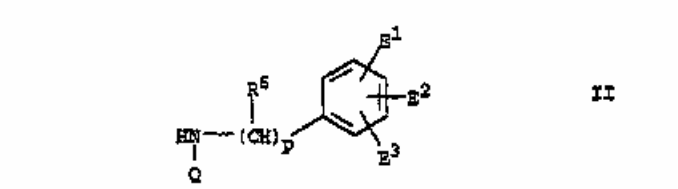
2.3.1 Compounds of formula I



I

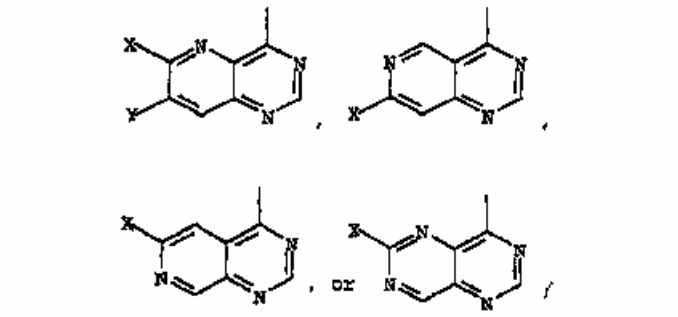
i.e. Claims 1 to 17, 48 (partially), 58 (partially), 61, 62, 63 (partially), 64 (partially), 65 (partially), 67 and 70 and their therapeutic applications, i.e. Claims 36, 39, 40, 45, 49, 54 and 55.

2.3.2 Compounds of formula II



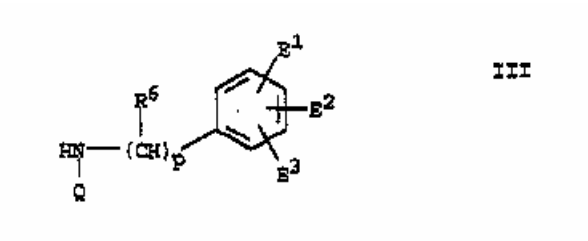
II

wherein Q is



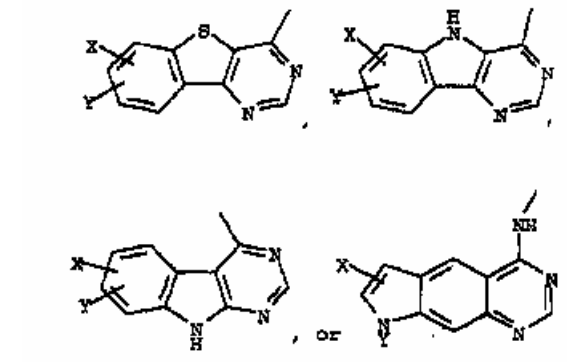
i.e. Claims 18 to 29, 48 (partially), 58 (partially), 59, 60, 63 (partially), 64 (partially), 66 and 69 and their therapeutic applications, i.e. Claim 37, and their use as a compound for the preparation of a pharmaceutical composition for treating a disease, i.e. Claims 41, 42, 46, 50, 53 and 56.

2.3.3 Compounds of formula III



III

wherein Q is



i.e. Claims 30 to 35, 48 (partially), 58 (partially), 61, 62, 67 and 70 and their therapeutic applications, i.e. Claims 38, 43, 44, 47, 51, 54 and 57.

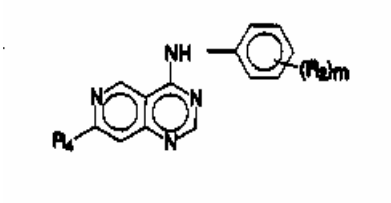
2.4 In view of the above, given the substantial differences between the three families of species (see point 2.3.1, 2.3.2 and 2.3.3 above), the conclusion of the Board concerning the novelty and inventive step of Claims 18 to 25, 66 and 69 would have no effect on the patentability of Claims 1 and 30 and related claims.

Since the appeal is only substantiated for Claims 18 to 25, 66 and 69, it cannot extend to Claims 1 and 30 and other claims related thereto. Nevertheless, the Board considers it proper to examine the other product subclaims depending from Claim 18, i.e. Claims 26 to 29, 48 (partially), 58 (partially), 59, 60, 63 (partially), 64 (partially); and claims related to therapeutic applications, i.e. Claim 37; and to claims for use of a compound for the preparation of a pharmaceutical for treating a disease, i.e. Claims 41, 42, 46, 50, 53 and 56 since the conclusions of the Board regarding the claims attacked will have an impact on these other subclaims (see G 9/91, loc.cit. point 11).

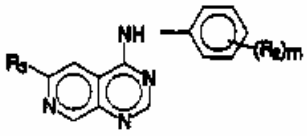
2.5 In conclusion the scope of the appeal is limited to the following claims as granted: to product Claim 18, dependent Claims 19 to 29, 48 (partially), 58 (partially), 59, 60, 63 (partially), 64 (partially), 66 and 69; therapeutic applications Claim 37; use of a compound for the preparation of a pharmaceutical for treating a disease Claims 41, 42, 46, 50, 53 and 56.

3. Novelty

3.1 Document (3), the sole disclosure cited by the Appellant against novelty discloses *inter alia* compounds of formula



and



wherein R_4 (first formula) and R_3 (second formula) can be lower alkoxy, amino or lower mono or dialkylamino, m = 0-3, R_2 is *inter alia* lower alkyl (1-4 carbon atoms) (see page 15, paragraphs 12, 13 and 14; page 16, formula and paragraphs 17, 18 and 19; and page 17, formula).

3.2 The Appellant contended that from a proper reading of Claim 18, it turned out that X when Y was absent could match five definitions, namely -D-E-F-, $-SR^4-$, $-OR^4$, $-NHR^3$ or hydrogen, in particular, when Q corresponded to the second and third structure (see point II above). The claim was clear and no reference to the description was necessary, let alone the fact that such an interpretation would not be proper since it would allow the proprietor of the patent to avoid the need to amend the claim and, therefore, to avoid the need to comply

with Article 123(2) EPC. It followed that the subject-matter of Claim 18 was anticipated by the disclosure of document (3) insofar as X meant OR^4 or $-NHR^3$.

3.3 The Board does not share the Appellant's view. The definition of X as put forward by the Appellant is exclusively set out **in relationship with** Y for the first formula of Q, i.e. a pyrido[3,2-d]pyrimidine cycle. No definition of X alone is given for the second, third and fourth formula of Q, i.e. pyrido[4,3-d]pyrimidine, pyrido[3,4-d]pyrimidine and pyrimido[5,4-d]pyrimidine respectively which relate to different kind of compounds.

3.4 By contrast, the Respondent argued that since the definition of X was not present, the skilled person had to find a definition which made sense and would have interpreted Claim 1 in view of the description in accordance with Article 69 EPC and its protocol of interpretation. As held by the Opposition Division, it was apparent from the description that all the claimed compounds had a Michael acceptor side-chain which, as a matter of fact, rendered the subject-matter novel over document (3). The decision T 416/87 (see OJ EPO 1990, 415) was cited in that respect.

3.5 Decision T 416/87 cited by the Respondent is not relevant since it relates to a case where the disputed feature was not **present** in the claim but only in the description. The substituent X, by contrast, is present in formula II in Claim 18 of the patent in suit.

The Board cannot, furthermore, accept the Appellant's submission that the skilled person in view of the

description in accordance with Article 69 EPC and its protocol on interpretation would have found that X was a Michael acceptor.

Article 69 EPC sets out that the extent of protection conferred by a European patent shall be determined by the terms of the claims. The purpose of the Protocol on interpretation of Article 69 EPC is to make clear that the extent of protection conferred is not limited to the strict literal meaning of the terms of the claims. Article 69 EPC and its Protocol do not provide a basis for excluding what is literally covered by the terms of the claims. Applying this to the present case, the Board considers it inconsistent with proper claim interpretation to read into the claim a particular meaning for X which only appears in the description and then to rely on this feature to provide a distinction over the prior art (see T 881/01, point 2.1, not published in the OJ EPO).

Furthermore, the extent of the protection of a patent is examined by the EPO in the opposition proceedings only within the framework of Article 123(3) EPC. The interpretation of the extent of the protection of a patent is not the task of the EPO, but, according to Articles 64 and 69 EPC, that of the national courts competent in procedures on infringement cases (see T 740/96 of 26 October 2000, point 3.3 and T 442/91 of 23 June 1994, point 3, both decisions not published in the OJ EPO). In particular, Article 69 EPC does not offer any basis for reading into a claim features which can be found in the description when judging novelty (see T 1208/97 of 3 November 2000, point 4(b), not published in the OJ EPO).

3.6 According to Article 84 EPC the claims define the matter for which protection is sought. The compounds of Claim 18 when Q is a pyrido[4,3-d]pyrimidine and a pyrido[3,4-d]pyrimidine heterocycle comprises X as a substituent. Indeed, X cannot be absent since the molecule would be unstable. In the absence of any precision as to the chemical nature of X, the sole conclusion is that it can have any definition that would appear sensible to the skilled person.

3.7 Document (3) discloses pyrido[4,3-d]pyrimidines or pyrido[3,4-d]pyrimidines wherein the substituents R_4 and R_3 may be lower alkoxy, amino or lower mono or dialkylamino (see point 3.1 above). The substituents R_4 and R_3 correspond to the X substituent of the claimed compounds wherein Q is a pyrido[4,3-d]pyrimidine and a pyrido[3,4-d]pyrimidine heterocycle respectively. The open definition of X encompasses the disclosed meanings of R_4 and R_3. It follows that the compounds disclosed in document (3) anticipate some of the compounds of Claim 18.

3.8 In view of the above, the compounds disclosed in document (3) being within the definition of Claim 18 properly understood (see points 3.1 and 3.6 above), the subject-matter of Claim 18 does not meet the requirements of Articles 52(1) and 54(1)(2) EPC.

3.9 Since the Board can only decide on a request as a whole, the main request of the Respondent is to be rejected.

Auxiliary request I

4. Amendments

4.1 Claim 19 results from the deletion in Claim 18 as granted of the compounds wherein Q is a pyrido[3,2-d]pyrimidine heterocycle (first formula) and the deletion of any meaning for X except -D-E-F-.

4.2 The Respondent argued that this amendment was supported by the application as filed and relied, in that respect, on the description (page 12) and Claim 18 as originally filed. However, the cited parts of the application as filed do not give any information on the meaning of X when Y is absent. In fact, X and Y are only defined **in relation with each other** when Q is pyrido[3,2-d]pyrimidine, now deleted. For the other remaining meanings of Q, the application as filed is silent concerning X and, therefore, the meaning X is -D-E-F- for the compounds of Claim 19 is not directly and unambiguously derivable from the application as filed. Claim 19 results from amendments which contravene Article 123(2) EPC and for this reason is to be rejected.

4.3 Since the Board can only decide on a request as a whole, auxiliary request I of the Respondent is to be rejected.

Auxiliary request II

5. Amendments

5.1 Although the scope of this appeal is restricted to the claims maintained by the Opposition Division as set out in point 2.5 above, it is to be examined whether the proposed set of claims of the present request meets in its entirety the requirements of Article 123(2)(3) (see G 9/91, OJ EPO 1993, 408, point 19) and whether the present request does not put the Opponent (the sole Appellant) in a worse situation than if it had not appealed (see G 1/99, OJ EPO 2001, 381, Order).

5.2 The subject-matter of Claims 1 to 17 finds support in Claims 1 to 17 as filed. The introduced disclaimer in Claim 1 aims to restore novelty over document (1) which is prior art under Article 54(3) and (4) EPC (see point III above) and is allowable. Due to the disclaimer, the subject-matter of Claims 1 to 17 represents a restriction with respect to Claim 1. The subject-matter of Claims 1 to 17 is identical to the subject-matter of Claims 1 to 17 as maintained by the Opposition Division.

The subject-matter of Claim 18 of the present request finds support in Claim 22 of the application as filed. The subject-matter of Claims 19 to 23 of the present request finds support in Claims 18, 22, 23, 24, 26, 27, 28 and 29 of the application as filed. The subject-matter of Claims 18 to 23 represents a restriction with respect to Claim 18 as granted and as maintained by the Opposition Division.

The subject-matter of Claims 24 to 29 of the present request finds support in Claims 30 to 35 as filed. It is identical to the subject-matter of Claims 30 to 35 as granted and as maintained by the Opposition Division.

The subject-matter of Claim 42 finds support in Claim 48 as filed. The deletion of some compounds does not lead to a particular class of compounds not disclosed originally. Furthermore, the introduction of N-[4-(3-chloro-4-fluoro-phenylamino)-quinazolin-6-yl]-acrylamide finds support in Claim 58 as filed. Claim 42 represents a restriction with respect to Claim 48 as granted and is identical to Claim 48 as maintained by the Opposition Division.

The subject-matter of Claim 52 finds support in Claim 58 as filed and differs therefrom by the deletion of N-[4-(3-chloro-4-fluoro-phenylamino)-quinazolin-6-yl]-acrylamide and its transfer to Claim 42 (see above paragraph). It represents a restriction with respect to Claim 58 as granted and is identical to Claim 58 as maintained by the Opposition Division.

The subject-matter of Claims 30 to 41, 43 to 51 finds support in Claims 36 to 47, 49 to 57 as filed respectively. Since those claims relate to therapeutic applications of the compounds according to Claims 1 to 17, 18 to 23 and 24 to 29, they do not extend beyond the protection of the patent as granted and the protection of the claims maintained by the Opposition Division.

The subject-matter of Claims 53 to 64 finds support in Claims 59 to 70 as filed. Since those claims relate to

compounds according to Claims 1 to 17, 18 to 23 and 24 to 29, they do not extend beyond the protection of the patent as granted and the protection of the claims maintained by the Opposition Division.

5.3 In conclusion, the amendments do not raise any objection under Article 123(2)(3) EPC and the set of claims resulting therefrom do not put the Opponent and sole Appellant in a worse situation than if it had not appealed (see G 1/99, OJ EPO 2001, 381, Order).

6. Scope of examination of substantive issues

In view of the scope of this appeal (see points 2.2, 2.4 and 2.5 above), the extent of examination of substantive issues is limited to the following claims of auxiliary request II:

Product claims

– Claims 18 to 23, 42 to the extent that this claim includes compounds under Claim 18, 52 to the extent that this claim includes compounds under Claim 18, 53, 54, 57 and 58 to the extent that these claims include compounds under Claim 18, 60 and 63.

Therapeutic application / Pharmaceutical composition claim

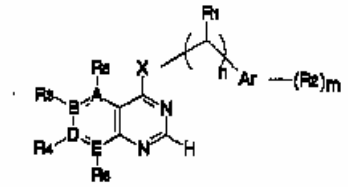
– Claim 31.

Use of a compound for the preparation of a pharmaceutical composition for treating a disease

– Claims 35, 36, 40, 44, 47, 50.

7. Novelty

7.1 Document (3) discloses fused heterocyclic pyrimidine derivatives capable of inhibiting tyrosine kinases of the epidermal growth factor receptor family of formula I which are useful in suppressing tumors,



Formula I

wherein *inter alia*
X is NH, Ar is phenyl, m = 0-3, R_2 is a defined substituent and
A is nitrogen with R_5 not present, B, D and E are carbon, R_3, R_4, are defined substituents and R_6 is hydrogen, to give a pyrido[3,2-d]pyrimidine heterocycle moiety, or
A, D and E are carbon, R_5, R_6 are hydrogen, R_4 is a defined substituent, B is nitrogen and R_3 not present, to give a pyrido[4,3-d]pyrimidine heterocycle moiety or
A, B and E are carbon, R_5, R_6 are hydrogen, R_3 is a defined substituent, D is nitrogen and R_4 not present, to give a pyrido[3,4-d]pyrimidine heterocycle moiety (see page 1, "Technical field"; page 6, second paragraph; pages 7 and 8).

7.2 The subject-matter of Claim 18 is distinguished from the disclosure of document (3) in that X or Y are -D-E-F- as defined in that claim. None of the definitions of R_3 or R_4 recited in document (3) overlap with the definition of X or Y as defined in Claim 18. For this reason Claim 18 is novel over the disclosure of document (3). The other product claims depending from Claim 18 are novel for the same reasons.

The subject-matter of Claim 22 distinguishes from the disclosure of document (3) in that X is an acrylamide substituent when Q is pyrido[4,3-d]pyrimidine and X is an acrylamide or ethenylsulfonamide substituent when Q is pyrido[3,4-d]pyrimidine. None of the definitions of R_3 or R_4 recited in document (3) overlap with the definition of X as defined in Claim 22. For this reason Claim 22 is novel over the disclosure of document (3).

7.3 Document (1), (which is prior art under Article 54(3) and (4) EPC), and document (2) disclose quinazoline derivatives and, therefore, do not anticipate the subject-matter of Claim 18 or 22. The other product claims depending from Claim 18 are novel for the same reason.

7.4 In view of the above, the claims considered (see point 6 above) meet the requirements of Article 54 EPC.

8. Inventive step

8.1 The patent in suit according to Claims 18 and 22 relates to irreversible inhibitors of tyrosine kinases and can be useful for treating various diseases *inter alia* cancers (see paragraph [0094] of the patent in suit and point II above).

8.2 The Board concurs with both parties that document (3) is the closest state of the art to define the technical problem to be solved since it aims at the same objective as the patent in suit (see point 7.1 above) and has the most relevant technical features in common, i.e. requiring the minimum of structural modifications

(see the Case Law of the Boards of Appeal of the EPO, 4th edition 2001, Section I. D. 3.1., "Determination of the closest prior art", page 102).

8.3 There is no evidence of beneficial effects or advantageous properties vis-à-vis the closest state of the art, i.e. document (3). Thus the technical problem to be solved is the provision of further fused heterocyclic pyrimidine derivatives that are useful for suppressing tumours and that are capable of irreversibly inhibiting tyrosine kinases of the epidermal growth factor receptor family.

8.4 The Appellant disputed that the technical problem was solved since Claim 18 covered tri-substituted phenyl compounds, i.e. in which E^1, E^2, E^3 are anything but hydrogen, whereas no experimental data had been provided to show a single compound encompassed by Claim 18 to be an irreversible tyrosine kinase inhibitor, far less to establish the activity across the scope of the claim. The burden of proof rested in that respect on the Proprietor of the patent.

8.4.1 The Board holds however that in the opposition/appeal proceedings when the technical problem is a simple alternative as in the present case, the presumption prevails that this problem is solved unless the Opponent (now Appellant) can raise a serious doubt as to the existence of the alleged technical effect. This is consistent with the character of the post-grant opposition proceedings under the EPC which are in principle to be considered as contentious proceedings between parties normally representing opposite interests. It is the responsibility of the Opponent

(now Appellant) to present the facts, evidence and arguments in support of the grounds on which the opposition is based (see T 671/03 of 20 July 2006, point 2.1.1 and T 270/90, OJ EPO 1993, 725, point 2.1).

8.4.2 The biological activity of the derivatives where Q is a pyrido[3,2-d]pyrimidin is illustrated by a sole working example, i.e. N-[4-(Bromo-phenylamino)-pyrido[3,2-d]pyrimidin-6-yl]acrylamide (see example 41, page 52 and Tables 1 and 2 of the patent in suit). In that example, the phenyl moiety is mono-substituted. However document (3) discloses in the same technical field that the biological activity of fused heterocyclic pyrimidine derivatives is not affected when the phenyl moiety is unsubstitued, mono-, di- or tri-substitued (see point 7.1 above, m = 0-3). The Appellant did not submit any evidence to the contrary. Therefore, the argument of the Appellant must fail for lack of substantiation and the Board considers plausible that the technical problem defined above is solved. The Board is also satisfied that the subject-matter of Claim 22 solves the technical problem defined above, in particular, in view of the examples 2, 35 to 40, and 48 to 52, for the same reasons.

8.5 It remains to be decided whether or not the claimed solution was obvious in view of the prior art cited.

8.5.1 The compounds of Claim 18 are, in particular, characterized in that the substituent X or Y is -D-E-F-. This substituent comprises a carbonyl or sulfonyl or -P(=O)(OR^2)- or sulfinyl directly linked to an unsaturation (double or triple bond). Document (3) does not give any hint towards compounds of formula I (see

point 7.1) having a pyrido[3,2-d]pyrimidine heterocycle moiety and the substituent R_3 or R_4 would have one of the meanings for X or Y, i.e. -D-E-F- defined in Claim 18. In particular, when R_3 or R_4 is carbonato (-OC(O)OR), R is lower alkyl or cycloalkyl (see page 8, line 34 to page 9, line 2). Likewise, document (3) does not give any hint towards compounds of formula I (see point 7.1) having a pyrido[4,3-d]pyrimidine heterocycle moiety or a pyrido[3,4-d]pyrimidine heterocycle moiety and the substituent R_4 or R_3 would have respectively one of the meanings for X as defined in Claim 22, namely an acrylamide or an ethenylsulfonamide. Document (2) relating to quinazoline derivatives cannot be combined with document (3) to solve the above technical problem. Document (1) is not prior art under Article 56 EPC (see point III above).

8.5.2 It derives therefrom that the person skilled in the art would not have been led in an obvious manner towards the claimed compounds according to Claim 18 or 22 in view of the prior art cited to solve the technical problem defined above. Claims 18 and 22 involve, therefore, an inventive step. The same applies to dependent Claims 19 to 21 and 23, 53, 54, 60 and 63; and for Claims 42, 52, 57 and 58 to the extent that these claims include compounds under Claim 18 or Claim 22. Claim 31 relating to a pharmaceutical composition that comprises a compound of anyone of claims 18 to 23 is based on the same inventive concept and derives its patentability on the same basis as do Claims 18 and 22. Claims 35, 36, 40, 44, 47 and 50 relating to the use of a compound for the preparation of a pharmaceutical composition for treating a disease are based on the same inventive concept and derive

their patentability on the same basis as do Claims 18 and 22.

8.5.3 In conclusion, the subject-matter of Claims 18 and 22 and the other claims considered (see point 6 above) complies with the requirements of Article 56 EPC.

Since the scope of appeal is limited to certain claims, (see points 2.5 and 6 above), and the Board is not required to examine, *ex officio*, the compatibility of the other claims with the EPC (see point 2.2. above), it follows that auxiliary request II is to be allowed.

9. Article 111(1) EPC - Remittal to the first instance

Although the Board has come to the conclusion that auxiliary request II was to be allowed, it was noted that the description had still to be brought into conformity with the claims of the present request. Therefore, having regard to the fact that the function of the Boards of Appeal is primarily to give a judicial decision upon the correctness of the earlier decision taken by the first instance, the Board exercises its discretion under Article 111(1) EPC to remit the case to the first instance in order for the description to be adapted to the allowable claimed subject-matter according to auxiliary request II submitted before the Board at the oral proceedings.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to maintain the patent with the following claims and a description to be adapted: Claims 1-64 of auxiliary request II dated 24 April 2007 received during oral proceedings of 24 April 2007.

The Registrar The Chairman

N. Maslin A. Nuss