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Case Number: T 2665/16 - 3.3.01

Application Number: 10747657.4

Publication Number: 2467724

IPC: G01N33/68

Language of the proceedings: EN

Title of invention:
SURVIVAL PROGNOSTIC ASSAY

Patent Proprietor:
The Binding Site Group Limited

Opponent:
Siemens Healthcare Diagnostics Products GmbH

Headword:
Survival prognostic assay/THE BINDING SITE GROUP

Relevant legal provisions:
EPC Art. 54(2), 56

Keyword:
Novelty - (yes)
Inventive step - (no)

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Case Number: T 2665/16 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 15 October 2021

Appellant I: (Patent Proprietor)	The Binding Site Group Limited 8 Calthorpe Road Edgbaston Birmingham B15 1QT (GB)
Representative:	Elsy, David Withers & Rogers LLP 2 London Bridge London SE1 9RA (GB)
Appellant II: (Opponent)	Siemens Healthcare Diagnostics Products GmbH Emil-von-Behring Strasse 76 35041 Marburg (DE)
Representative:	Siemens Healthcare Diagnostics Products GmbH Patents and Licenses Postfach 22 16 34 80506 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 20 October 2016 concerning maintenance of the European Patent No. 2467724 in amended form**

Composition of the Board:

Chairwoman	R. Hauss
Members:	T. Sommerfeld
	L. Bühler

Summary of Facts and Submissions

I. European patent No. 2467724 is based on European patent application No. 10747657.4, which was filed as an international application and published as WO 2011/021041. The patent is entitled "Survival prognostic assay" and was granted with 11 claims.

II. An opposition to the granted patent was filed, the opponent requesting revocation of the patent in its entirety on the grounds of lack of novelty and inventive step (Articles 54(2) and 56 EPC and Article 100(a) EPC), lack of sufficiency of disclosure (Article 100(b) EPC) and added subject-matter (Article 100(c) EPC).

III. In an interlocutory decision announced at oral proceedings, the opposition division found that the patent could be maintained in amended form on the basis of auxiliary request 5, which had been filed on 27 September 2016 during oral proceedings (Articles 101(3)(a) and 106(2) EPC).

The opposition division considered that the set of claims of the main request (claims as granted) fulfilled the requirements of Article 123(2) EPC (Article 100(c) EPC) and Article 83 EPC (Article 100(b) EPC) but not those of Article 54 EPC (Article 100(a) EPC), while the sets of claims of auxiliary requests 1 to 4 all fulfilled the requirements of Article 123(2) EPC but not those of Article 54 EPC.

IV. The patent proprietor and the opponent both lodged an appeal against that decision.

V. Oral proceedings before the board took place by videoconference, as agreed by both parties.

During the oral proceedings, appellant I (patent proprietor) withdrew auxiliary request 2. At the end of oral proceedings the chairwoman announced the board's decision.

VI. The claims of the **main request** are the claims as granted. Claim 1 reads as follows:

"1. A general health screen method comprising detecting an amount of free light chains (FLC) in a sample from a subject and comparing this to a predetermined value, wherein a lower amount of FLC is associated with increased survival and/or better general health of the subject, and a higher level of FLC indicates the possible presence of an undetected medical problem."

Claim 1 of **auxiliary request 1** differs from claim 1 of the main request in that the following feature was added at the end of the claim: "..., wherein the subject does not have apparent symptoms of a life threatening disease."

Claim 1 of **auxiliary request 3** differs from claim 1 of the main request in that it was amended as shown:

"1. A general health screen method comprising detecting an amount of free light chains (FLC) in a sample from a subject and comparing this to a predetermined value, wherein a lower amount of FLC is associated with increased survival ~~and/or better general health~~ of the subject and a higher level of FLC indicates the possible presence of an undetected medical problem."

Claim 1 of **auxiliary request 4** combines the amendments of auxiliary requests 1 and 3.

Claim 1 of **auxiliary request 5** differs from claim 1 of the main request in that it was amended as shown:

"1. A general health screen method comprising detecting an amount of free light chains (FLC) in a sample from a subject and comparing this to a predetermined value, wherein a lower amount of FLC is associated with increased survival ~~and/or better general health~~ of the subject, ~~and a higher level of FLC indicates the possible presence of an undetected medical problem~~ wherein the subject does not have apparent symptoms of a life threatening disease."

Claim 1 of **auxiliary request 6** differs from claim 1 of the main request in that it was amended as shown:

"1. A general health screen method comprising detecting ~~an~~ the amount of total free light chains (FLC) in a sample from a subject and comparing this to a predetermined value, wherein a lower amount of FLC is associated with increased survival ~~and/or better general health~~ of the subject, and a higher level of FLC indicates the possible presence of an undetected medical problem."

VII. The documents cited during the proceedings before the opposition division and the board of appeal include the following:

D2 Hutchinson C.A. et al. 2008, Expert Opin. Ther. Targets 12(6):667-676

D4 Hopper J.E. et al. 1989, J. Clin. Immunol. 9(4): 338-350

D9 http://medical-dictionary.thefreedictionary.com/general+health+screen>general health screen<

D10 Marks H.H. 1965, A.J.P.H. 55(3):416-423

VIII. The submissions of appellant I, in so far as they are relevant to the present decision, may be summarised as follows.

Novelty

Claim 1 of the main request was novel over document D2 because D2 disclosed the use of the test for patient follow-up in the context of a pre-existing condition, while the test as claimed was directed to a general health screen method within the definition given in document D9. As explained in paragraph [0013] of the patent, the claimed method was not a diagnostic test for a particular disease. The further feature "undetected medical problem" specified that the general health screen was for subjects who did not have a diagnosed disease, and not subjects with detected medical conditions. D2 disclosed the use of the test for diagnosing an existing problem, namely for identifying kidney disease in patients with a predetermined disease, diabetes. Moreover, D2 did not disclose any link between the test result and survival.

Inventive step

D2 related to diabetes and taught the detection of FLC as a marker of a predetermined condition. There was no suggestion, either in D2 or in the remaining prior art, that FLC could be used as a marker in a general health screen method, as in claim 1 of the main request. The final paragraph of D2 in fact taught that FLC would not be a suitable marker for outcome prediction.

Claim 1 of auxiliary request 1 comprised the additional feature that "the subject does not have symptoms of a life threatening disease". This feature was not part of the prior art and there was no suggestion of using FLC as a marker in subjects without a life-threatening disease such as diabetes.

The same arguments applied, mutatis mutandis, to auxiliary requests 3 and 4.

As for claim 1 of auxiliary request 5, this was restricted to the alternative that lower FLC indicated increased survival. Long-term survival had not been assessed in the prior art; the inventors were the first to do so.

Claim 1 of auxiliary request 6 was further restricted to the measurement of total FLC, while document D2 only disclosed measurement of kappa and lambda FLCs individually.

IX. The arguments of appellant II (opponent), in so far as they are relevant to the present decision, may be summarised as follows.

Novelty

The expression general health screen method meant that the method could be used to examine the state of health of a subject, regardless of whether there was a pre-existing condition. Patients with pre-existing conditions, such as those of D2, were not excluded. D2 taught that the amount of FLC was suitable for indicating the presence of undetected medical problems, namely kidney disease. While the patients of D2 were

known to have diabetes, they were not known to have kidney disease: this was thus an undetected medical problem that could be detected by measuring FLC. As to the link to survival, although it was not explicitly stated in D2 it was implicit there, since the absence of medical problems implicitly indicated that there was a higher probability of survival.

Inventive step

Starting from document D2 as closest prior art, there was nothing to prevent the skilled person from using a general health screen method in diabetic patients as well. The technical problem would be the examination of the general state of health in diabetic patients, and the skilled person would include a test of FLC as part of a general health screen in diabetic patients, in particular in view of the teaching of D2 (e.g. abstract, last 5 lines).

The same arguments also applied to claim 1 of auxiliary requests 1, 3 and 4. The feature "subject does not have apparent symptoms of a life threatening disease" in auxiliary requests 1 and 4 did not mean that the subject was free of disease. Diabetic patients did not necessarily have any symptoms, let alone symptoms of a life-threatening disease.

As for auxiliary request 5, D2 did not explicitly refer to survival but taught that a higher FLC level was linked to a medical problem while a lower FLC level was linked to an absence of a medical problem, which would generally mean that the subject had a better prognosis, including increased survival. This was also the way that the patent proprietor had interpreted its results. Moreover, diabetic kidney disease was known as a common

death risk among diabetic patients (D10, tables 5 and 6).

Claim 1 of auxiliary request 6 specified that total FLC was measured, which was not disclosed in D2 but was disclosed in D4. In D2, kappa and lambda FLCs were detected separately, but it was stated that both were increased, so the skilled person would conclude that the same results were to be expected when measuring the total FLC.

X. Appellant I (patent proprietor) requested that the decision under appeal be set aside and that the opposition be rejected (main request) or, in the alternative, that the patent be maintained in amended form on the basis of the claims of auxiliary request 1 (filed by letter dated 1 December 2015) or auxiliary request 3 or 4 (both filed by letter dated 26 August 2016) or, in the alternative, that the opponent's appeal be dismissed and that the patent be maintained in amended form on the basis of the claims of auxiliary request 5 (filed during oral proceedings on 27 September 2016) or, in the alternative, that the patent be maintained in amended form on the basis of the claims of auxiliary request 6 (filed as auxiliary request 5 by letter of 26 August 2016).

Appellant II (opponent) requested that the decision under appeal be set aside and that the patent be revoked.

Reasons for the Decision

1. The appeals are admissible.

Main request

2. Article 54 EPC

2.1 Document D2 discloses a method for examining the state of health of a patient, which comprises determining the amount of FLC in a sample from the subject (page 670, table 2: serum samples from healthy and diabetic patients) and comparing the amount with a predetermined value (page 670, table 2 and right-hand column, second paragraph), wherein an increased amount of FLC is indicative of the probable presence of an as yet unidentified medical problem, namely diabetic kidney disease (abstract and page 671, left-hand column). Diabetic kidney disease is known as a common death risk among diabetic patients (D10, tables 5 and 6) and also increases the risk of cardiovascular disease (D2, page 667, last paragraph), which is also accompanied by an increase in death risk. Hence, an increased risk of diabetic kidney disease implies that the patient also has an increased risk of death, meaning a decreased survival rate.

2.2 The board agrees with appellant II that D2 teaches that the detection of higher FLC levels in diabetic patients is indicative of the presence of an as yet undetected medical problem, namely renal disease. Furthermore, although not explicitly stated in D2, the FLC levels can be interpreted as also being indicative of decreased (in the case of higher levels) or increased (in the case of lower levels) patient survival because,

as argued by appellant II, the presence of a medical problem is associated with a poorer prognosis, which is ultimately reflected in a decrease in patient survival.

2.3 However, the board considers that the disclosure of D2 is different from the claimed subject-matter, because it does not describe the detection of FLC levels in the context of a general health screen method, as specified by the claim. Although, as argued by appellant II, a general health screen method can also be performed in patients with pre-existing conditions, such a method is not disclosed in D2, which instead discloses the detection of FLC levels with the purpose of diagnosing a specific medical condition, namely renal disease. The same test as that claimed is used, but in circumstances which are different from those recited in the claim.

2.4 Hence, the board comes to the conclusion that the subject-matter of claim 1 of the main request is novel over the disclosure of D2 (Article 54(2) EPC).

3. Article 56 EPC

3.1 It was not in dispute that document D2 is a suitable starting point in the prior art for the assessment of inventive step. The difference from the subject-matter of claim 1, as discussed above under novelty, is that D2 does not disclose the use of the method as claimed in the context of a general health screen. The technical effect of said difference is that a general state of health of the patient is detected, rather than just one specific medical condition. The objective technical problem can thus be formulated as the provision of a method for examination of the general state of health of a diabetic patient. The board is convinced that the problem has been solved by the

claimed solution, which involves combining the test with further screening methods by integrating it into a general health screen.

3.2 However, the board considers that the claimed solution is obvious. It is common general knowledge that diabetic patients have a number of potential complications in different organs that can increase patient morbidity and mortality. One such complication is renal disease. Document D2 teaches that, since type II diabetes patients may have raised concentrations of serum and urinary polyclonal FLCs before overt renal disease occurs, this finding could provide a useful tool for early diagnosis of diabetic kidney disease (abstract, last 5 lines). As renal disease is not the only complication which may occur, the skilled person (in the present case a physician) would be aware of the need to monitor the general state of health of such patients in order to detect any as yet undiagnosed medical problem as early as possible. Moreover, the skilled person would particularly consider including tests that are suitable for early diagnosis of common complications of the underlying disease. Hence, with the purpose of examining the general state of health of the patient, the skilled person would arrive at the solution of integrating the FLC detection test disclosed in D2 into the battery of tests which make up a general health screening (as defined in D9) as a matter of routine.

3.3 The board thus comes to the conclusion that the subject-matter of claim 1 of the main request does not involve an inventive step (Article 56 EPC).

4. Auxiliary request 1 - Article 56 EPC

4.1 Claim 1 of auxiliary request 1 differs from claim 1 of the main request in that the method is to be used on a subject who does not have apparent symptoms of a life-threatening disease.

4.2 While diabetes can be considered a life-threatening disease, the additional feature of auxiliary request 1 does not distinguish the claimed subject-matter from the disclosure of D2, because there is no teaching in D2 that the diabetic patients studied have symptoms of any kind, let alone of a life-threatening disease. The fact that a subject has been diagnosed as a diabetic does not mean that the subject necessarily displays any symptoms: on the contrary, it is to be expected that diagnosed patients will undergo therapy that suppresses any potential symptoms.

4.3 The board thus comes to the conclusion that claim 1 of auxiliary request 1 also relates to subject-matter that lacks inventive step (Article 56 EPC).

5. Auxiliary requests 3 and 4 - Article 56 EPC

5.1 Claim 1 of auxiliary request 3 differs from claim 1 of the main request in that the feature of "better general health" has been deleted, while claim 1 of auxiliary request 4 combines the amendments of auxiliary requests 1 and 3.

5.2 The feature that a higher amount of FLC indicates the presence of an undetected medical problem is still part of claim 1 of these requests. Hence, for the same reasons as for the main request and auxiliary

request 1, the claims of these requests do not involve an inventive step (Article 56 EPC).

6. Auxiliary request 5 - Article 56 EPC

6.1 Claim 1 of auxiliary request 5 differs from claim 1 of auxiliary request 1 in that it only comprises the alternative "wherein a lower amount of FLC is associated with increased survival". As was explained by appellant I in the context of novelty, this feature is to be interpreted as meaning that a lower amount of FLC is associated with increased survival by comparison with subjects displaying higher FLC levels.

6.2 The board agrees with the arguments of appellant II that, according to D2, a lower amount of FLC is indicative of the absence of a (further, as yet undetected) medical problem, which implies a better prognosis and therefore increased survival.

6.3 Hence, the board comes to the conclusion that claim 1 of auxiliary request 5 also lacks inventive step (Article 56 EPC).

7. Auxiliary request 6 - Article 56 EPC

7.1 Claim 1 of auxiliary request 6 differs from claim 1 of auxiliary request 3 in that it specifies that total FLC is measured.

7.2 Document D2 does not disclose measurement of the amount of total FLC but rather of kappa and lambda FLC separately. However, D2 states that both FLC types correlated with all tested markers of renal disease (abstract, lines 10 and 11), so the skilled person would conclude that the same results were to be

expected when measuring total FLC. Moreover, tests for measuring total FLC were available in the prior art, as evidenced by D4, which discloses the measurement of total FLC as a predictive clinical marker (abstract). In the absence of any arguments from appellant I as to why the measurement of total FLC rather than of kappa and lambda FLC should be of any advantage, the board considers that this is simply an obvious, equally suitable alternative.

7.3 The board thus comes to the conclusion that claim 1 of auxiliary request 6 does not involve an inventive step either (Article 56 EPC).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairwoman:

M. Schalow R. Hauss

Decision electronically authenticated