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Datasheet for the decision of 14 December 2021

Case Number: T 2744/16 - 3.3.01

Application Number: 11180207.0

Publication Number: 2420838

IPC: G01N33/574

Language of the proceedings: EN

Title of invention:
An in vitro method for the prognosis of progression of a cancer and of the outcome in a patient and means for performing said method

Patent Proprietor:
INSERM (Institut National de la Santé et de la Recherche Médicale)

Opponent:
Ventana Medical Systems, Inc.

Headword:
Cancer prognosis method/INSERM

Relevant legal provisions:
EPC Art. 123(2), 56

Keyword:
Amendments - allowable (no: MR, AR1 and AR2)
Inventive step - (no)

Decisions cited:
T 1506/13, T 0208/17, T 1264/19, T 0377/14, T 0344/89

Catchword:

Europäisches Patentamt
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Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

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Case Number: T 2744/16 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 14 December 2021

Appellant: (Patent Proprietor)	INSERM (Institut National de la Santé et de la Recherche Médicale) 101, rue de Tolbiac 75013 Paris (FR)
Representative:	Cabinet Becker et Associés 25, rue Louis le Grand 75002 Paris (FR)
Appellant: (Opponent)	Ventana Medical Systems, Inc. 1910 Innovation Park Dr. Tucson, AZ 85755 (US)
Representative:	Mewburn Ellis LLP Aurora Building Counterslip Bristol BS1 6BX (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 14 November 2016 concerning maintenance of the European Patent No. 2420838 in amended form**

Composition of the Board:

Chairman	A. Lindner
Members:	T. Sommerfeld
	R. Romandini

Summary of Facts and Submissions

I. European patent No. 2 420 838 is based on application 11180207.0, a divisional application of European patent application 06809203.0. The parent application was filed as an international application and published as WO 2007/045996. The patent is entitled "An in vitro method for the prognosis of progression of a cancer and of the outcome in a patient and means for performing said method" and was granted with five claims.

II. Opposition was filed against the granted patent, the opponent requesting revocation of the patent in its entirety on the grounds of lack of novelty and inventive step (Articles 54(2), 56 and 100(a) EPC) and lack of sufficiency of disclosure (Article 100(b) EPC).

III. By an interlocutory decision announced at oral proceedings, the opposition division decided that the patent be maintained in amended form on the basis of the set of claims of the first auxiliary request filed by letter of 12 May 2016 (Articles 101(3)(a) and 106(2) EPC).

The opposition division considered that the claims according to the main request lacked inventive step, while they were found to fulfil the requirements of Articles 123(2), 54 and 83 EPC.

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

V. With the statement of the grounds of appeal, the appellant-patent proprietor requested that the decision of the opposition division be set aside and that the

patent be maintained in amended form according to the main request presented during opposition proceedings or, alternatively, according to one of auxiliary requests 1 to 3, all filed with the grounds of appeal (auxiliary request 3 being identical to the auxiliary request which the opposition division considered allowable).

VI. With the statement of the grounds of appeal, the appellant-opponent requested that the decision be set aside and that the patent be revoked in its entirety. New documents D12 to D16 were submitted.

VII. With its reply to the opponent's grounds of appeal, the appellant-patentee filed a new auxiliary request 2 and renumbered the previous auxiliary requests 2 and 3 as 3 and 4, respectively.

VIII. With its reply to the patent proprietor's grounds of appeal, the appellant-opponent requested that the new auxiliary requests filed by the appellant-patentee with the statement of grounds of appeal not be admitted into the proceedings.

IX. Summons for oral proceedings before the board were issued followed by a communication pursuant to Article 15(1) RPBA, providing a preliminary opinion on some issues, in particular admission of claim requests and documents.

X. By letter dated 6 December 2021, the appellant-patent proprietor withdrew the pending auxiliary request 3 so that auxiliary request 4 became auxiliary request 3.

XI. Oral proceedings before the board took place by videoconference, with the agreement of both parties. At

the end of the oral proceedings, the chairman announced the board's decision.

XII. Claim 1 of the **main request** reads as follows:

"1. An *in vitro* method for the prognosis of patients for progression of a cancer, which method comprises the following steps:
a) quantifying, in a tumor tissue sample from said patient, one or more biological markers indicative of the status of the adaptive immune response of said patient against cancer; and
b) comparing the value obtained at step a) for said one or more biological markers with a predetermined reference value for the same biological markers; which predetermined reference value is correlated with a specific prognosis of progression of said cancer,
wherein said one or more biological markers comprise integrin alpha E (ITGAE)
wherein said cancer is selected from the group consisting of adrenal cortical cancer, anal cancer, bile duct cancer (e.g. periphilar cancer, distal bile duct cancer, intrahepatic bile duct cancer), bladder cancer, brain and central nervous system cancer (e.g. meningioma, astocytoma [*sic*], oligodendrogliomas, ependymoma, gliomas, medulloblastoma, ganglioglioma, Schwannoma [*sic*], germinoma, craniopharyngioma), breast cancer (e.g. ductal carcinoma in situ, infiltrating ductal carcinoma, infiltrating lobular carcinoma, lobular carcinoma in situ, gynecomastia), cervical cancer, colorectal cancer, endometrial cancer (e.g. endometrial adenocarcinoma, adenocanthoma, papillary serous adnocarcinoma [*sic*], clear cell), esophagus cancer, gallbladder cancer (mucinous adenocarcinoma, small cell carcinoma), gastrointestinal carcinoid tumors (e.g. choriocarcinoma, chorioadenomadestruens),

Kaposi's sarcoma, kidney cancer (e.g. renal cell cancer), laryngeal and hypopharyngeal cancer, liver cancer (e.g. hemangioma, hepatic adenoma, focal nodular hyperplasia, hepatocellular carcinoma), lung cancer (e.g. small cell lung cancer, non-small cell lung cancer), mesothelioma, plasmacytoma, nasal cavity and paranasal sinus cancer (e.g. esthesioneuroblastoma, midline granuloma), nasopharyngeal cancer, neuroblastoma, oral cavity and oropharyngeal cancer, ovarian cancer, pancreatic cancer, penile cancer, pituitary cancer, prostate cancer, retinoblastoma, rhabdomyosarcoma (e.g. embryonalrhabdomyosarcoma, alveolar rhabdomyosarcoma, pleomorphic rhabdomyosarcoma), salivary gland cancer, skin cancer (e.g. melanoma, nonmelanoma skin cancer), stomach cancer, testicular cancer (e.g. seminoma, nonseminoma germ cell cancer), thymus cancer, thyroid cancer (e.g. follicular carcinoma, anaplastic carcinoma, poorly differentiated carcinoma, medullary thyroid carcinoma), vaginal cancer, vulvar cancer, and uterine cancer (e.g. uterine leiomyosarcoma)."

Claim 1 of **auxiliary request 1** differs from claim 1 of the main request in that gynecomastia, plasmacytoma and midline granuloma have been deleted from the list of cancers.

Claim 1 of **auxiliary request 2** differs from claim 1 of the main request in that schwannoma, gynecomastia, plasmacytoma and midline granuloma have been deleted from the list of cancers.

Auxiliary request 3 is identical to the first auxiliary request considered allowable by the opposition division. Claim 1 differs from claim 1 of the main

request in that the cancer has been limited to colorectal cancer.

XIII. The documents cited during the proceedings before the opposition division and the board include the following:

D3	Quinn E *et al.* 2003, Eur. J. Cancer 39, pp. 469-475
D6	Sobin LH 2001, Cancer Supplement 91(8), pp. 1589-1592
Appendix A	Experimental report (11 pages), submitted 14 April 2015

XIV. The submissions of the appellant-patent proprietor, in so far as they are relevant to the present decision, may be summarised as follows.

Article 123(2) EPC: main request and auxiliary requests 1 and 2

Throughout the application as filed, it was clear that solid tumours were meant. For example, page 46, lines 10 to 15, teaching the core of the invention, stated that "the inventors believe that the cancer prognosis method of the invention may be successfully carried out for prognosing the progression of any cancer that develops from a central tumor to which cells from the immune system have access". The skilled person would thus immediately understand that the invention related to solid tumours, i.e. to organ tumours, and not to liquid tumours. This was further evidenced by other passages of the application as filed such as page 15, lines 8 to 15, and page 16, lines 20 to 27, referring to "the center of the tumor"; page 19, lines 15 to 22, and page 20, line 5, referring to "tumor tissue

sample"; and page 24, lines 15 to 19, referring to "tumor site". In claim 1 of the main request, a small number of pathologies were deleted from the original list. These were essentially Castleman disease, which was a benign disease and therefore did not fit into the claim, which specifically referred to cancers; and Hodgkin and non-Hodgkin's lymphoma, which were liquid cancers. This deletion derived from the general teaching, which was directed to solid cancers. No new group was disclosed, as was apparent when applying the novelty test. The combination of the marker and the claimed diseases was not a novel disclosure over the disclosure of the application as filed. T 1506/13 defined the conditions allowing deletion of elements of a list as being that the group must remain a generic group not distinct from the original group and that no new invention should be created. These criteria were met by the case at issue, where only a limited number of pathologies was deleted, and the group remaining was still a generic group, distinct from the original only by being smaller. The facts were analogous to those underlying T 208/17, in which the board acknowledged that deletion of elements from a list did not add subject-matter.

Article 56 EPC: auxiliary request 3

D6 was the closest prior art and was directed to a prognostic method based on TNM ("tumour-node-metastasis"). While D6 referred to other prognostic factors, these were to be used in conjunction with TNM (see last page, right column, first sentence). The technical problem was the provision of a non-anatomical prognostic marker reliable on its own without needing TNM and having greater selectivity and sensitivity than the TNM staging method. Appendix A showed the

superiority of using CD103 (Table 1 on page 2). The skilled person would have to select integrins from Table 2 of D6, but integrins were a very large family, and, in any case, D6 did not at all suggest exploring in this direction. D3 did not serve to establish CD103 as a prognostic factor of colorectal cancer and did not allow concluding that CD103 was a prognostic marker independent of the cancer status. Only with hindsight could D6 be combined with D3 and not with a reasonable expectation of success of arriving at the invention, in particular not with the prognostic value obtained by the inventors.

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

Article 123(2) EPC: main request and auxiliary requests 1 and 2

Claim 1 was not directed to a generic group of solid tumours, as argued by the patent proprietor, but rather to a list of individualised cancers and to CD103 not as a sole marker but as one of one or more markers. CD103 was not prioritised in the application as filed and only on page 47 was there a reference to "at least one biological marker", otherwise it was always "two or more markers". CD103 was one of many markers listed in the application and was selected from that list and combined to a second list which had been adapted to overcome later specified prior art. The list of claim 1 differed from the list of page 46 in that a number of pathologies were deleted, thus singling out a new invention not disclosed in the application as filed. Contrary to the arguments of the patent proprietor, a new group of cancers was singled out and combined with

a non-prioritised marker to create a new invention. While the passages indicated by the patent proprietor might refer to solid tumours, there was no teaching to adapt the general list by removing liquid tumours.

Article 56 EPC: auxiliary request 3

Document D6 was a review of the well-established TNM classification system, and it disclosed further prognostic factors on page 1591 and in Table 2. In Table 2, integrins were mentioned. The difference was the use of the integrin CD103 as a particular biological marker. The problem was to provide a specific non-anatomic marker from the list of further prognostic markers in Table 2 of D6 for prognosis assessment of colorectal cancer. D3, also related to colorectal cancer, showed that CD103 was a marker for MSI. D3 moreover taught that MSI had higher numbers of CD103+ IELs ("intraepithelial lymphocytes"), this being a hallmark of an adaptive immune response. There was thus a link between D6, looking at prognostic factors for colorectal cancer (Table 2), and D3, teaching CD103 as a marker in a type of colorectal cancer which had a good prognosis. Claim 1 did not exclude the use of other prognostic factors or methods such as TNM.

XVI. The appellant-patent proprietor requested that the appealed decision be set aside and that the patent be maintained in amended form according to the main request presented during opposition proceedings or, alternatively, according to auxiliary request 1 filed with the grounds of appeal or auxiliary request 2, filed with letter of reply to the opponent's grounds of appeal or, alternatively, that the opponent's appeal be dismissed (auxiliary request 3).

XVII. The appellant-opponent requested that the appealed decision be set aside and that the patent be revoked in its entirety.

Reasons for the Decision

1. The appeals are admissible.

Main request

2. Article 123(2) EPC

2.1 Claim 1 of the main request derives from the combination of granted claims 1 and 4, differing in that some pathologies have been deleted from the list of granted claim 4.

2.2 As to a basis in the application as filed, the following is noted, reference being made to the application as published (EP 2420838 A2).

2.2.1 The preamble and steps a) and b) of claim 1 of the main request are almost verbatim to item 1 on page 93.

2.2.2 The feature "wherein said one or more biological markers comprise integrin alpha E (ITGAE)" has no verbatim basis in the application as filed but reference to this marker (ITGAE, also designated CD103) is found in the following passages of the application as published: paragraphs [0166], [0187], [0192], [0272], [0277] and [0332]; Table 3 on page 42; Table 9 on page 70; and items 14 and 15 on pages 94 and 95. In all these passages, the ITGAE/CD103 marker is listed among a number of other markers. Of these passages, however, paragraphs [0187], [0192], [0272] and [0277]

cannot serve as basis because they are either in the context of an embodiment comprising "a combination of 2 or more distinct biological markers" (paragraphs [0187] and [0192]), or disclose antibodies directed against the biological markers (paragraph [0272] and Table 3) or kits comprising primers hybridising with the corresponding nucleic acids (paragraph [0277]). In the remaining passages, the ITGAE/CD103 marker is one among 78 "various biological markers" in paragraph [0166]; one among five "markers of T cell migration" listed in paragraph [0332], which also lists another 11 markers related to T lymphocytes; one among 630 markers (according to the invitation to pay additional fees pursuant to Article 17(3)(a) and Rule 40.1 PCT by the International Searching Authority in relation to the parent application) in Table 9; one of 78 "various biological markers" in item 14(i), item 14 comprising a further six groups of markers; and one of almost 400 markers in item 15.

2.2.3 The list of pathologies is disclosed in paragraph [0164]. The list of pathologies in the claim differs from the list in this passage in that some pathologies have been deleted. From the original list of 47 cancers (or groups of cancers), bone cancer, Castleman disease, Hodgkin's disease and non-Hodgkin's lymphoma are no longer present in claim 1 of the main request.

2.3 As argued by the appellant-opponent, nowhere in the application as filed is it disclosed that CD103 is a preferred marker. To the contrary, this marker is listed in long lists of other markers, as discussed above, no preference being given to any of them. Hence, the selection of this marker is a selection of one embodiment - which is not given as preferred - from several long lists.

2.4 On the other hand, the list of diseases in the claim has not been disclosed as a group in the application as filed. Instead, a longer list is disclosed, as discussed above, from which four elements have been deleted. The deletion of these four elements, which were present in claim 4 as granted, was done to overcome opposition grounds, namely novelty (deletion of bone cancer) and sufficiency of disclosure (deletion of Castleman disease, Hodgkin's disease and non-Hodgkin's lymphoma). As regards to the deletion of Castleman disease, Hodgkin's disease and non-Hodgkin's lymphoma, the appellant-patent proprietor argued that these cancers were deleted because they were either not cancer (Castleman disease) or they were not solid tumours (Hodgkin's disease and non-Hodgkin's lymphoma). According to the appellant-patent proprietor, the remaining group was a generic group of solid tumours, and it was apparent from the whole of the application that the invention was directed to such a generic group of solid tumours.

2.5 The board disagrees. The skilled person would have not implicitly and unambiguously derived from the application as filed that a generic group of solid tumours was envisaged. Indeed, the application as filed states that the invention "relates to the field of prognosis of the outcome of a cancer in a patient" (e.g. paragraph [0001]). Throughout the application, reference is made to cancer in general, and in particular to colorectal cancer, which is also the cancer further investigated in the examples. In paragraph [0163], it is stated that "Although the cancer prognosis method according to the invention has been tested for colorectal cancer, said method may be applied for a wide variety of cancers". A list of

cancers for which "the cancer prognosis method according to the invention is potentially useful" is given in paragraph [0164], as discussed above. However, there is no teaching that these cancers should be solid tumours, nor would this be implicit from the list, which also includes non-solid tumours and even non-cancer pathologies.

2.6 As reviewed in decision T 1506/13, point 4.2, deletion of elements from a list is allowable if it fulfils two cumulative conditions.

- First, the deletion must not single out any previously not specifically mentioned individual compound or group of compounds, and the remaining subject-matter must be maintained as a generic group of compounds differing from the original group only by its smaller size.
- Second, the deletion must not lead to a combination of a specific meaning not originally disclosed, i.e. it must not generate another invention, or, in other words, it must merely restrict the required protection and not provide any technical contribution to the originally disclosed subject-matter.

2.7 In the board's view, neither of these two conditions is fulfilled. The deletion of the four elements from the longer list of cancers singles out a group of cancers, solid cancers, which had not been specifically mentioned previously. Hence, a new group is created which does not differ from the original group only by its smaller size. Furthermore, the deletion generates another invention.

2.8 Claim 1 of the main request is thus directed to subject-matter that results from the combination of one

selected element from long lists, for which there is no pointer in the application as filed, with a subgroup (hence a further selection) from another long list, for which again there is no pointer. Moreover, the new subgroup consists, according to the appellant-patent proprietor, of a group of solid tumours for which the prognostic method of the invention would be enablingly disclosed in the application as filed. The board considers that such a combination is not disclosed in the application as filed and results in the creation of a new invention also not derivable from the application as filed.

2.9 The appellant-patent proprietor referred to a number of passages in the application as filed from which it would be implicit that solid tumours were meant. It argued that expressions such as "cancer that develops from a central tumor to which cells from the immune system have access", "center of the tumor" (...), "tumor tissue sample" (...) and "tumor site" (...) would render apparent that the invention was concerned with solid and not liquid tumours. The board agrees that these passages may all be interpreted as referring to solid tumours. However, these are just exemplary embodiments of how to put the invention into practice. The board fails to see any teaching in the application as filed towards the group of solid tumours.

2.10 The board thus disagrees that the current case is similar to that underlying T 208/17, where the board in question concluded that the two conditions for deletion of elements from a list were fulfilled. As is apparent from points 2.2 and 2.3 of that decision, all eight elements (mutations) originally in the list were considered equal alternatives, so that the deletion of two of them merely resulted in a shorter list of equal

alternatives and did not generate a new invention because the six remaining mutations as a group had no functionality different from that of the individual mutations of the original group. This is, as explained above, not given in the case at hand.

2.11 The board thus concludes that claim 1 of the main request does not fulfil the requirements of Article 123(2) EPC.

Auxiliary request 1

3. Admission

3.1 The appellant-opponent requested that this request, filed with the appellant-patent proprietor's grounds of appeal, not be admitted into the proceedings. In its communication pursuant to Article 15(1) RPBA, the board indicated that it saw no reason to exclude auxiliary request 1 from the appeal proceedings. The appellant-opponent provided no further comments.

3.2 The board decided that auxiliary request 1 was not to be excluded from the proceedings (Article 12(4) RPBA 2007). However, in view of the outcome of the present decision, the board sees no reason to further substantiate the decision on this point and merely refers to its preliminary opinion in the communication under Article 15(1) RPBA.

4. Article 123(2) EPC

4.1 Claim 1 of auxiliary request 1 differs from claim 1 of the main request solely in that gynecomastia, plasmacytoma and midline granuloma have been deleted from the list of cancers.

4.2 According to the appellant-patent proprietor, this amendment was a reaction to the opponent's arguments that these pathologies could not be considered "solid cancers".

4.3 The board considers that claim 1 of auxiliary request 1 contravenes Article 123(2) EPC for the same reasons as for claim 1 of the main request. As extensively discussed above, the remaining group represents a new group which had not been disclosed as such in the application as filed, let alone in combination with the use of the specifically claimed marker CD103.

Auxiliary request 2

5. Admission

5.1 The current auxiliary request 2 was filed by the appellant-patent proprietor with the reply to the opponent's grounds of appeal, and the appellant-opponent raised no objections concerning admission of this request. The board also saw no reason to exclude auxiliary request 2 from the appeal proceedings, as was explained in the communication under Article 15(1) RPBA.

5.2 The board thus decided not to exclude auxiliary request 2 from the proceedings. However, in view of the outcome of the present decision, the board does not find it necessary to substantiate this part of the decision.

6. Article 123(2) EPC

6.1 Claim 1 of auxiliary request 2 differs from claim 1 of the main request solely in that gynecomastia,

plasmacytoma, midline granuloma and schwannoma have been deleted from the list of cancers.

6.2 As for auxiliary request 1, this request was filed in reaction to the opponent's arguments that these pathologies could not be considered "solid cancers".

6.3 Hence, for the same reasons as put forward above in relation to the main request and auxiliary request 1, claim 1 of auxiliary request 2 does not meet the requirements of Article 123(2) EPC.

Auxiliary request 3

7. Article 56 EPC

7.1 Auxiliary request 3 is identical to the first auxiliary request considered allowable by the opposition division. Claim 1 differs from claim 1 of the higher ranking requests in that the cancer is defined as being colorectal cancer.

7.2 The current patent is related to "the prognosis of the outcome of a cancer in a patient, which prognosis is based on the quantification of one or several biological markers that are indicative of the presence of, or alternatively the level of, the adaptive immune response of said patient against said cancer" (paragraph [0002]). According to the patent, "most of the currently known markers of cancer are poorly reliable", and there is therefore a "need for reliable diagnostic and prognostic tools" (paragraph [0003]). The patent discusses the limitations, in particular in the case of colorectal cancer, of the generally used classification system for malignant tumours, TNM ("tumour-node-metastasis"), which serves

as a basis for selection of appropriate therapy and for prognostic purposes, and of the Duke's classification system, which is also used for colorectal cancers (paragraphs [0004] and [0005]). The aim of the patent is to provide "improved methods of prognosis of the outcome of cancers, including colorectal cancers, that would stage the disease in a more accurate and a more reliable way than the presently available methods, that is essentially, if not exclusively, clinicopathological staging methods" (paragraph [0025]).

7.3 Document D6, which is also concerned with the prognosis of cancer (see Title and abstract) and in relation to colorectal cancer (Table 2), is the closest prior art. Document D6 discusses the TNM system and its established role in the assessment of cancer prognosis and discloses further prognostic factors specifically related to colorectal cancer in Table 2. Among these further prognostic factors are integrins, under the heading of "possible factors". The difference to the claimed subject-matter is that a method for prognosis assessment based on quantification of integrins, let alone the specific integrin ITGAE/CD103, is not disclosed in D6. The technical effect of this difference is, according to the patent (paragraph [0030]), that "a precise determination of the *in situ* adaptive immune response to malignant cancers, and especially to colorectal cancers, can be used as the sole parameter for predicting the subsequent clinical outcome of cancer-bearing patients, regardless of the extent of local tumor invasion and spread of regional lymph nodes". Example 2 provides evidence for this statement. The technical problem can thus be formulated as the provision of an alternative method for the assessment of prognosis of colorectal cancer. The

solution is the method as claimed, and the board is satisfied that the problem has been solved.

7.4 Motivated to provide an alternative prognostic method for colorectal cancer and prompted by D6 to explore further prognostic factors such as integrins, among others, the skilled person would turn to documents dealing with biological markers of colorectal cancer. D3, which studies the phenotype of given subtypes of colorectal cancer, would be such a document. D3 teaches that a subtype of colorectal cancer, namely colorectal cancers with microsatellite instability (MSI), harbour increased numbers of $CD8^+CD103^+$ intraepithelial lymphocytes ("IELs") (D3, abstract and passage spanning pages 472 and 473). D3 moreover teaches that the MSI colorectal phenotype is associated with improved prognosis and suggests that this effect on prognosis may be attributed to the high numbers of IELs in MSI colorectal cancers (page 469, right column, last paragraph). The skilled person would thus learn from D3 that CD103 is associated with the improved prognosis of a subtype of colorectal cancers, namely MSI colorectal cancers. They would thus conclude that CD103 could be a promising biomarker for use in an alternative prognosis method for colorectal cancers and that they would just have to perform the appropriate, routine testing to assess its validity for this purpose. Hence, the skilled person would arrive at the claimed invention in an obvious way when starting from D6 and combining the teaching of D3.

7.5 The board disagrees with the appellant-patent proprietor's formulation of the technical problem as the provision of a non-anatomical prognostic marker reliable on its own without needing TNM and having greater selectivity and sensitivity than the TNM

staging method. Such advantages over the closest prior art are not disclosed or suggested in the patent, which only teaches the use of biological markers as a precise and reliable alternative to the TNM system. Even if the post-published data of Appendix A (Table 1 on page 2) is considered to show that the claimed method was superior to the prior-art method based on TNM, such an effect was not shown or even suggested in the application as filed for any of the many markers listed, let alone for ITGAE/CD103. Nor is this derivable from the general statement in paragraph [0030] (see point 7.3 above), which only indicates that the method of the invention can be used independently of anatomic methods but not that it is better than the anatomic methods. While the objective technical problem does not have to be explicitly disclosed in the application as filed, it must at least be foreshadowed (see T 1264/19, point 20; T 377/14, point 2.1.5; and T 344/89, point 5.3.1).

7.6 As to obviousness, the appellant-patent proprietor essentially argued that nothing in D6 would induce the skilled person to replace anatomic criteria with the measure of a biological marker indicating the status of the adaptive immune response; that D3 did not disclose a correlation between ITGAE and an improved prognosis; that D3 failed to disclose that ITGAE represents a suitable marker for determining the survival of colorectal cancer patients whatever the status of the cancer (MSI/MSS); and that it cannot be derived from D3 that the expression of the gene might provide better information on the prognosis of the patient in comparison with the standard classification (i.e. UICC TNM).

7.7 It is true that D6 discusses the TNM system as the basis for prognosis assessment of cancer and that it envisages that other methods (e.g. further prognostic factors) may complement this system "without losing the vital anatomic content of TNM" (D6, page 1592, right column, first sentence). However, the board notes that claim 1 of auxiliary request 3 is not restricted to using solely the CD103 marker as a prognostic factor but instead allows that other methods (including TNM) or markers be used. This is also consistent with the disclosure of the application as a whole, which does not teach or provide support for the use of CD103 as the sole marker. Instead, it teaches to use a panel of markers indicative of the immune adaptive response. D6 also does not point to the specific integrin ITGAE/ CD103 but instead only indicates the family of integrins as possible prognostic factors. However, even without this reference in D6, the skilled person, motivated to look for alternative prognostic indicators in colorectal cancers, would turn to documents disclosing the detection of biomarkers in this type of tumours, such as D3. Contrary to the arguments of the appellant-patent proprietor, D3 does in fact establish a link between ITGAE/CD103 and an improved prognosis because it teaches that this marker is harboured by cells present in higher number in a subtype of colorectal cancer that has a better prognosis. As to the argument that D3 does not allow concluding that ITGAE/CD103 represents a suitable marker for determining the survival of colorectal cancer patients whatever the status of the cancer (MSI/MSS), the board notes that the claimed subject-matter is directed to colorectal cancer in general, thus including all its subtypes. Whether the ITGAE/CD103 marker is an universal prognostic marker for all subtypes of colorectal cancers is not relevant. D3 suggests that

the detection of CD103+ cells in colorectal cancer is linked to a subtype with better prognosis, and therefore it can be concluded that CD103 can be used as a prognostic marker.

7.8 Finally, while it cannot be derived from D3 that the expression of the gene might provide better information on the prognosis of the patient in comparison with the standard classification (i.e. UICC TNM), the same is true for the patent, which, as discussed above (point 7.5), only teaches the use of biological markers as a precise and reliable alternative to the TNM system but not as a better prognostic method.

7.9 The board thus concludes that claim 1 of auxiliary request 3 lacks inventive step (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 Chairman:

M. Schalow A. Lindner

Decision electronically authenticated