EXHIBIT G

However, the earlier application, document D15, did not contain SEQ ID NO: 13 of document D16 but only a Figure 9 showing a partial DNA sequence which was identical to SEQ ID NO: 13 of document D16 except for that it lacked the two guanine residues at the 3' end.

When answering the question whether or not the skilled person may have recognized the DNA of SEQ ID NO. 13 and of Figure 9 of document D15 as representing the "same subject-matter" and, thus, the "same invention" within the meaning of Article 87 EPC, as required in the Opinion G 2/98 (supra), the Board decided that the presence of two additional guanine residues in SEQ ID NO: 13 resulted in a different molecule that was not directly and unambiguously derivable from the earlier application, so that the priority right was not validly claimed.

25. Decision T 30/02 refers in point (15) of the reasons to decision T 923/92 (OJ EPO 1996, 564).

In this earlier decision the Board decided that a claim referring to a process comprising the preparation of a protein which was defined by its function and by an amino acid sequence 1 to 527 as depicted in Figure 5, did not enjoy priority from documents (P1) and (P2) which contained a Figure 5 that differed from Figure 5 of the patent in suit in respect of three amino acid positions 175, 178 and 191.

In point (16) of the decision the Board stated, that the primary amino acid sequence of a protein (or the nucleotide sequence of a DNA) constituted a true

technical feature and relying on a given sequence rather than on another one for the definition of the subject-matter of an invention in a claim made a critical difference.

In point (13), the Board commented on the relevance of decision T 65/92 (this decision is relied upon by the Appellant I in the present case in order to substantiate his line of argumentation (see point (28) below)) in the following way:

"In decision T 65/92 (supra), the board decided that a difference in the reported upper limit of the molecular weight of the glycosylated form of a polypeptide between the priority document and the European patent application (all other measured parameters being identical) did not reflect a true structural difference between the products of the two applications, especially in view of the fact that the molecular weight is able to be determined only approximately. Contrary to that, in the present case, the primary structure of human t-PA is not a parameter which is determined approximately, unless one relies on a general formula, which is not the case here."

26. The present Board endorses the decisions discussed in points (22) to (25) above, taking into account the technical situation underlying each individual case.

It has to be decided whether or not the specific technical situation in the present case requires the Board to develop, as Appellant I put it, "a more pragmatic approach" with regard to the issue of

priority rights concerning the concept of "the same invention".

27. Indeed, Appellant I, in the written procedure and during oral proceedings, submitted various arguments why the Board in the present case should not follow the gist of the decisions discussed in points (22) to (25) above, but should come to the conclusion that the BRCA1 coding sequence disclosed in the application as filed enjoys priority from priority document (P2), although it deviates from the BRCA1 coding sequence disclosed in priority document (P2) by 15 nucleotide residues.

28. Appellant I provided calculations, showing that the 5592 nucleotides (including stop codon) of the coding sequences of BRCA1 according to priority document (P2) and the application as filed shared a sequence identity of 99,73%. He argued that "silent mutations" would not generally be expected to disrupt protein function, so that the actually relevant sequence identity referred to 9 deviations out of 5592 nucleotides, i.e. 99,84%.

Appellant I took the view, that, if parameters (here: the nucleic acid sequence) which are used to define a substance (here: a nucleic acid) in a claim are known to vary within margins of commonly encountered experimental errors, the occurrence of variation in such a parameter between a disclosure in a priority document and the corresponding later application did not necessarily abrogate entitlement to the claimed priority. Appellant I referred in this respect to decision T 65/92 of 13 June 1993, wherein the Board acknowledged the entitlement to the claimed priority for a claim referring to a protein defined by reference

to its molecular weight, although the molecular weight ranges in the priority document and in the claim under consideration were not identical. The difference in molecular weight was considered to fall within the experimental error of the method for determination and was considered to have no influence on the fact that the priority document and the patent application related in substance to the same subject-matter. A similar approach had been taken in decision T 1147/98 of 14 July 2000.

Appellant I argued, that DNA sequencing was a measuring method which regularly produced experimental errors and was unable to produce 100% accurate data. This was acknowledged for example in documents D164 to D166, wherein it was stated that, although the sequence accuracy of so-called "finished sequences" should be no less than 99,99%, also preliminary results of sequencing projects were very useful, so that such "working drafts" having sequence accuracy between 90 and 99% should also be published. Therefore, as DNA sequencing had a certain margin of experimental error this should be taken into account when considering the validity of a priority claim directed to subject-matter referring to a DNA sequence. Legal certainty for third parties, an issue relied upon by Appellant II, was considered to be a function of the technology it referred to and the need for it could not be higher than experimental certainty.

The skilled person was aware of the possibility of sequencing errors and would have realized that the BRCA1 coding sequence of priority document (P2), containing two ambiguities ("N" at positions 1571 and

4535), was a preliminary version from which he/she would have been able to inevitably arrive at the correct sequence by using routine methods, like PCR, library screening, or sub-cloning.

As it was clear that a skilled person would have interpreted priority document (P2) and the application as filed as relating in substance to the same BRCA1 coding sequence, the sequence deviations did not negatively affect entitlement to the claimed priority date.

29. The argument, that a claim which explicitly refers to a **DNA sequence comprising a coding sequence for a specific polypeptide** should be entitled to claim priority from an earlier application disclosing a DNA sequence deviating from the claimed one within the margin of error of the used sequencing method, is not compatible with the EBA's conclusion in Opinion G 2/98 (supra) that the requirement for claiming priority of "the same invention", referred to in Article 87(1) EPC, means that priority of a previous application in respect of a claim in a European patent application in accordance with Article 88 EPC is to be acknowledged only if the skilled person can derive the subject-matter of the claim directly and unambiguously, using common general knowledge, from the previous application as a whole.

Indeed, also decision T 70/05 (supra) has applied the principles set out in the Opinion of the EBA G 2/98 (supra), and held that no priority right can be claimed from an earlier application disclosing an amino acid or nucleotide sequence which differs from the sequence in

a later application only by unintended sequencing or typing errors.

Furthermore, with regard to Appellant I's reflections on the interrelation between legal certainty and experimental certainty, the Board considers that the acknowledgement of an "allowable" margin of error for a specific detection method would be open for interpretation and would lead to ambiguity and vagueness.

30. Appellant I argued that the nucleic acid of claim 1 was a tool for diagnosis of predisposition to breast or ovarian cancer. In order to assess whether the claims were entitled to claim priority from priority document (P2), it had to be established whether priority document (P2) in this respect disclosed the same invention as defined in the claims of auxiliary request II. Thus, it had to be decided whether priority document (P2), despite its reference to the deviated amino acid sequence of SEQ ID NO: 2, disclosed in an enabling form the same diagnostic tool as defined in claim 1 of auxiliary request II.

The technical problem underlying the patent in suit was the provision of the isolated BRCA1 gene as a tool to diagnose a predisposition to breast or ovarian cancer. The sequence deviations between priority document (P2) and the application as filed were irrelevant for solving this problem since in more than 180.000 tests carried out in the past twelve years there had never been allocated any relevance for the diagnosis of breast or ovarian cancer predisposition. Moreover, as soon as the inventors had published the BRCA1 coding

sequence in October 1994 in document D1, which sequence corresponds to the "deviating" sequence disclosed in priority document (P2), other scientists, using this sequence, were able to provide accurate detection of BRCA1 mutations and diagnosis of predisposition to breast and ovarian cancer. This was evident from the disclosure in documents D3, D4 and D17, all published before the present inventors revised the BRCA1 coding sequence to be identical to the one disclosed in the application as filed.

31. The Board emphasizes again that claims 1 and 2 refer to a DNA sequence comprising a coding sequence for a specific polypeptide.

To adopt the approach, that a decision on whether or not a claim to a DNA sequence in respect of "the same invention" as a priority document disclosing a deviating DNA sequence, can only be taken after it has been decided whether the deviations have an effect on the function of the claimed DNA sequence (here: as a diagnostic target or tool), is not compatible with the Opinion G 2/98 (supra) of the EBA, which stated in point (9) of the reasons for the decision that, making a distinction between technical features which are related to the function and effect of the invention and technical features which are not, with the possible consequence that a claimed invention is considered to remain the same even though a feature is modified or deleted, or a further feature is added, is inappropriate and prejudicial to a proper exercise of priority rights.

The Board considers, that a narrow interpretation of the concept of "the same invention" equating it with the concept of "the same subject-matter", as developed by the EBA, is the correct approach to take. Thus, the Board considers, that the DNA sequence disclosed in SEQ ID NO: 1 and the amino acid sequence deduced therefrom disclosed in SEQ ID NO:2 of priority document (P2) do not refer to "the same invention" as the DNA sequence and the amino acid sequence disclosed in SEQ ID NOs: 1 and 2 of the application as filed.

32. Appellant I argued that the respective technical situation in the decisions cited in points (22) to (25) above (i.e. decision T 923/93, T 351/01, T 30/02 and T 70/05) was fundamentally different from the situation underlying the patent in suit.

Decision T 923/93 (supra) only referred to deviations in the amino acid sequence of a protein having a defined biological function. In the case underlying decision T 30/02 (supra) two additional guanine residues resulted in the encoded xylanase being structurally different. No evidence had been provided that this structural difference did not cause a functional difference. Decision T 70/05 (supra) was concerned with a case which contained no information concerning the effect of sequence deviations between a prior art document and its priority document. Finally in case T 351/01 (supra) the Board was confronted with deviations between a polynucleotide sequence in the patent and in the priority documents, wherein said deviations were in the non-coding part. However in the case underlying decision T 351/01 (supra), as well as in all other cases, the parties had not put forward

arguments about the origin and the lack of relevance of the deviations.

Thus, the present case differed from all these cases in so far as Appellant I had provided arguments that the deviations were within the margin of error of the sequencing method and that said deviations had no effect on the successful use of the DNA sequence in diagnosis of cancer in 180.000 cases.

33. The Board repeats that the Opinion of the EBA G 2/98 (supra) held, that an approach which makes a distinction between technical features which are related to the function and effect of an invention and technical features which are not is problematic, can give rise to arbitrariness and is therefore inappropriate and prejudicial to a proper exercise of priority rights.

This principle has been followed in decisions concerning the field of DNA technology (see points (22) to (25) above). In decision T 351/01 (supra) the Board denied the right to priority in a case where the sequence deviations between the priority document and the patent were situated in the non-coding region, thus not having any effect on the sequence and thus function of the encoded protein. In decision T 70/05 (supra) it was explicitly stated, that no priority right could be claimed from an earlier application disclosing an amino acid or nucleotide sequence which differs from the sequence in a later application only by unintended sequencing or typing errors.

The submission of arguments referring to this issue, which according to Appellant I distinguishes the present case from the cases discussed above, is not automatically considered as proof that the Opinion G 2/98 and the case law of the Boards of appeal applying it are based on an incorrect interpretation of the law.

34. Furthermore, the Board observes that the case law of the Boards of Appeal with regard to the entitlement to priority of a claim referring to a nucleotide or amino acid sequence is uniform and definite. The arguments presented by Appellant I, therefore, cannot convince the Board that there is a special situation involved in the underlying case which could justify a deviation from this case law. Accordingly, the Board arrives at the decision that the subject-matter of the claims of Appellant I's auxiliary request II is only entitled to claim priority from the fifth priority document (P5), (US 409305; 24 March 1995).

Novelty (Article 54 EPC)

35. As a consequence of the above decision on right to priority document D1 belongs to the state of the art under Article 54(2) EPC.

At the oral proceedings, Appellant I stated that document D1 was novelty destroying for the subject-matter of claim 1 of auxiliary request II.

In view of this statement the Board sees no reason to further examine the claims of this request.

Referral of questions to the EBA (Article 112(1)(a) EPC)

36. Appellant I requested to refer the following questions to the EBA according to Article 112(1)(a) EPC:

"(1) If a priority document and a European patent application as filed concern the same physical entity but describe it in deviating form relying on the same physical characterisation method, can a claim to the physical entity enjoy priority under Article 87 EPC since it relates to the same invention according to G 2/98, when said descriptions only deviate within the margin of error of the physical characterization method employed at the time when the physical entity was characterized?

(2) More precisely, if a claim defines an invention by reference to a nucleotide sequence (or an amino acid sequence translated therefrom) does this subject-matter enjoy priority under Article 87 EPC as interpreted by G 2/98 from a disclosure in a priority document of a nucleotide sequence (or amino acid sequence translated therefrom) differing to an extent which is within the margin of error of the sequencing method employed at the time the nucleotide sequence was determined, provided that there is no reasonable doubt with regard to the physical identity of the molecule described in the priority document and referred to in the claim under consideration?

(3) If the answers to questions 1 and 2 are no, are the answers any different if it has been established that the deviations are technically irrelevant for the use of the invention in normal practice?"

37. Article 112(1)(a) EPC stipulates that the Board of Appeal, following a request from a party to the appeal, shall refer any question to the EBA if it considers that a decision is required in order to ensure uniform application of the law, or if an important point of law arises.

38. The questions proposed by Appellant I do not relate to a uniform application of the law, as this Board does not take a view of the law which would deviate from earlier cases (see points (22) to (25) above).

39. The second alternative according to Article 112(1)(a) EPC concerns the possibility of questions to be referred to the EBA in case there exists an important point of law.

Question (1) as formulated by Appellant I relies on the hypothesis that the "**same physical entity**" described in a priority document and in a European patent application in deviating form, relying on the same method of characterization, relates to "**the same invention according to G 2/98**", when said deviating description only results from the margin of error of the physical characterization method. Based on this assumption it is asked whether a claim to the physical entity in the European patent application can validly claim priority from the priority document.

This question, in a more precise form, is repeated in question (2), where the answer is made dependent on the further hypothetical provision "**... that there is no reasonable doubt with regard to the physical identity**

of the molecule described in the priority document and referred to in the claim under consideration."

In question (3) it is asked whether the answers to questions (1) and (2) depend on whether or not the deviations are technically relevant, which in the present case means, whether or not the deviations have an influence on the ability of BRCA1 to be used as a diagnostic tool.

40. The EBA in its Opinion G 2/98 (supra) has already decided that a narrow and strict interpretation of the concept of "the same invention" is to be applied, equating it with the concept of "the same subject-matter" referred to in Article 87(4) EPC. The EBA in its Opinion did not provide any basis for speculation that this narrow interpretation should, in a specific technical field, be replaced by an approach which takes into consideration possibly unintended errors resulting from specific physical characterization methods. Moreover the EBA has stated that a distinction between technical features which are related to the function and effect of the invention and technical features which are not is problematic and has to be avoided.

41. Questions that are based on hypothetical considerations are not suitable for a referral (cf decision T 118/89 of 19 September 1990). Furthermore, no referral based on questions already decided by the EBA can be permitted (cf decision T 82/93, OJ EPO 1996, 274).

In view of the above, Appellant I's request for referral of questions to the EBA is refused.

Auxiliary request III (Claims as maintained by the Opposition Division)

Amendments (Articles 123(2)(3) and 84 EPC)

42. The Board considers that the probe with the nucleotide sequence specified in claim 1 is directly and unambiguously derivable from the application as filed, particularly from page 4, lines 31 and 32 of the published version. The skilled person would understand this passage as referring to the numbering of the sequence presented in SEQ ID NO: 1, particularly in view of page 13, lines 50 to 51 stating that the "coding sequence for a BRCA1 polypeptide is shown in SEQ ID NO: 1", and claim 13 of the application as filed. The sequences of SEQ ID NOs: 35, 38, 41, 42, 47, 57, 62, 67, 72 and 81 are directly and unambiguously derivable from Table 9 on pages 44 and 45 of the application as published.

Claims 1 to 3, therefore, comply with Article 123(2) EPC.

As the subject-matter of claims 1 to 3 has been restricted in comparison to that of the claims as granted, the requirements of Article 123(3) EPC are also met.

The claims are clear and supported by the description as required by Article 84 EPC.

Patentable inventions (Article 52(2)(a) EPC)

43. It has been submitted by the Opponents that the sequences of the probes according to claim 1 occur in nature and are therefore a discovery rather than an invention. In view of Article 52(2) EPC, said probes were thus not patentable. During the oral proceedings, this point was not further pursued by any of the Opponents.

44. According to the case law of the Boards of Appeal (see decision T 272/95 of 23 October 2002), Article 52(2)(a) EPC is to be interpreted in accordance with the implementing Rule 23e(2) EPC which states:

"(2) An element isolated from the human body or otherwise produced by means of a technical process including the sequence or partial sequence of a gene may constitute a patentable invention, even if the structure of that element is identical to that of a natural element".

45. Claims 1 to 3 relate to nucleic acid **probes** comprising partial DNA sequences of the human BRCA1 gene, which are described in the patent in suit as having been obtained by technical processes (see especially page 5, paragraph [0024], and Table 9). These probes are thus isolated elements of the human body as defined in Rule 23e(2) EPC and thus patentable subject-matter. Accordingly, the subject-matter of claims 1 to 3 does not fall within the category of inventions which may not be patentable as being discoveries (Article 52(2)(a) EPC).

Exceptions to patentability (Article 53(a) EPC)

46. Appellant II and Opponent 02 presented different lines of argumentation why the claimed subject-matter was excluded from patentability under Article 53(a) EPC.

47. Appellant II submitted that no proof had been provided by Appellant I that the donors of the cells that had been critical to identify the BRCA1 gene had given a previous informed consent to the use of said cells. In the opinion of Appellant II, such previous informed consent would have had to include an explicit consent to the commercial exploitation of the research results by patents as well as a benefit sharing agreement, in particular with respect to members of kindreds 2082 and 2080, the cell donations of which had been essential in arriving at the claimed invention. In the absence of such proof, it had to be assumed that the initial obtaining of these research results involved severe ethical violations, and thus a violation of "ordre public" or morality as referred to in Article 53(a) EPC.

48. The Board observes that the EPC contains no provision establishing a requirement for applicants to submit evidence of a previous informed consent or a benefit sharing agreement. According to Rule 23b(1) EPC, the Directive 98/44/EC on the Legal Protection of Biotechnological Inventions (document D173; hereafter referred to as "the Directive") shall be used as a supplementary means of interpretation of the relevant provisions of the Convention and of Chapter VI ("Biotechnological inventions") of Part II of the Implementing Regulations. Recital (26) of the Directive states:

"Whereas if an invention is based on biological material of human origin or if it uses such material, where a patent application is filed, the person from whose body the material is taken must have had an opportunity of expressing free and informed consent thereto, **in accordance with national law**" (emphasis added by the Board).

49. The legislator has thus not provided for a procedure of verifying the informed consent in the framework of the grant of biotechnological patents under the EPC.

50. The Court of Justice of the European Communities in the judgment in case C-377/98 dated 9 October 2001 concerning the application for annulment of the Directive by the Kingdom of the Netherlands, supported by Italy and Norway (document D174) has dealt with a similar argument. There the applicant had submitted in its fifth plea that the absence in the Directive of a provision requiring verification of the consent of the donor or recipient of products obtained by biotechnological means undermined the right to self-determination. The Court rejected this plea stating that reliance on the fundamental right of human integrity was "clearly misplaced as against a directive which concerns only the grant of patents and whose scope does not therefore extend to activities before and after that grant, whether they involve research or the use of the patented products" (point (79) of the judgment). The Court furthermore stated that "[t]he grant of a patent does not preclude legal limitations or prohibitions applying to research into patentable products or the exploitation of patented products, as the 14th recital of the preamble to the Directive

points out. The purpose of the Directive is not to replace the restrictive provisions which guarantee, outside the scope of the Directive, compliance with certain ethical rules which include the right to self-determination by informed consent" (point (80) of the judgment).

The Board furthermore notes that also the "Opinion of Advocate General Jacobs" delivered on 14 June 2001 in case C-377/98 (document D175), stated in point (211) that "[i]n my view, however, although the requirement of consent to all potential uses of human material may be regarded as fundamental, patent law is not the appropriate framework for the imposition and monitoring of such a requirement".

51. Accordingly, the Board does not accept Appellant II's argument that the claimed subject-matter is not patentable under Article 53(a) EPC.

52. Opponent 02 argued that the socio-economic consequences of the patenting of the claimed subject-matter should be considered by the Board under Article 53(a) EPC, because in the present case, these consequences touched ethical issues. Patenting of the claimed subject-matter would not only result in increased costs for patients, but would also influence the way in which diagnosis and research would be organized in Europe, which would be clearly to the detriment of patients and doctors. The fact that a particular group of patients, i.e. patients suspected to carry a predisposition to breast cancer, would be faced with severe disadvantages and would become dependent on the patent proprietor, was contrary to human dignity. Therefore, the claimed subject-matter

constituted an exception to patentability under Article 53(a) EPC.

53. In order to deal with the objection of Opponent 02 it is helpful to look at the pertinent wording of Article 53(a) EPC:

"European patents shall not be granted in respect of inventions the... exploitation of which would be contrary to "ordre public" or morality...".

It is important to note that Article 53(a) EPC refers to the "exploitation of the invention", not about the "exploitation of the patent".

The objections raised by Opponent 02 are directed to the possible consequences of the exploitation of the patent in suit. It thus seems that such an objection, which goes to the exploitation of the patent and not to the exploitation of the invention, does not fall within Article 53(a) EPC. Thus, Opponent 02's objections under Article 53(a) EPC must be rejected upon this basis.

In an attempt to evade this legal consequence of the wording of Article 53(a) EPC, Opponent 02 sought to argue that the exploitation of the patent, in this case, could be assimilated to the exploitation of the invention, and thus the exploitation of the patent *per se* was contrary to "ordre public" and morality. Opponent 02 stressed that this invention concerned breast and ovarian cancer and had a significant impact on public health, thus in these special circumstances the Board should apply Article 53(a) EPC to the exploitation of the patent. The Board accepts that

public health care is a sensitive area, however the Board sees no basis in the EPC to distinguish in this respect between inventions concerning different technical fields. Such an approach has been confirmed by the EBA in its decision G 1/98 (OJ EPO 2000, 111; point (3.9) of the reasons) where the EBA stated that the EPO has not been vested with the task of taking into account the economic effects of the grant of patents in specific areas and restricting the field of patentable subject-matter accordingly.

In the Board's opinion the possible consequences of exploitation of the patent identified by Opponent 02 are the result of the exclusionary nature of the rights granted by a patent, that is the right to stop competitors from using the invention.

The objection of Opponent 02, reduced to its essence, is that the inevitable consequences of the exploitation of the patent in suit are contrary to "ordre public" or morality. Logically, such an objection applies to the exploitation of any patent, as the nature of the consequences of the exploitation of a patent (which derive from the exclusionary nature of private property rights), are the same for all patents.

Thus, for the reasons stated above, the Board rejects this objection.

54. Opponent 02 has further argued that the implementation of the Directive in the national law of France and Germany had made it clear that socio-economic and ethical concerns about the patenting of human genes had to be taken into account. The French legislator had

explicitly provided that not genes as such, but only functions derived from genes should be patentable, and the German legislator had provided a separate legislation for the patenting of human genes in view of ethical concerns.

55. Opponent 02 therefore seems to imply that the correct implementation of the Directive requires the importation of socio-economic concerns into the text of the Directive, upon the basis that certain EU member states have adopted this approach to implementing the Directive.

The Board does not agree with this position. The content of national legislation does not form part of the legal order established by the EPC and is thus irrelevant to the issue of how the EPC should be interpreted.

Opponent 02 also referred to the resolution of the European Parliament, P6_TA(2005)0407 of 26 October 2005 "Patents on biotechnological inventions" ("the Resolution"). Opponent 02 argued that the Resolution could be used to interpret the Directive and thus introduce socio-economic and ethical issues into the EPO's patent granting process.

Opponent 02 referred in the Oral Proceedings, in particular, to recitals J and L and paragraphs 4 and 5 of the Resolution. These state:

"J. whereas the Directive allows the patenting of human DNA only in connection with a function, but it is unclear whether a patent on DNA covers only

the application in this function or whether other functions are also covered by the patent,

L. whereas over-generous granting of patents can stifle innovation,

4. Considers that the Directive provides the framework for this in most cases, but that it still leaves important questions open, such as the patenting of human DNA;

5. Calls on the European Patent Office and the Member States to grant patents on human DNA only in connection with a concrete application and for the scope of the patent to be limited to this concrete application so that other users can use and patent the same DNA sequence for other applications (purpose-bound protection)".

Recitals J, L and paragraph 4, can be considered as general statements of fact and/or opinion. Paragraph 5 is the only part of the Resolution relied on by Opponent 02 that calls for action on the part of the EPO. The wording of paragraph 5 contains no suggestion that the EPO has been, or should be, vested with the task of taking into account the socio-economic effects of the grant of patents in specific areas and restricting the field of patentable subject-matter accordingly. Thus the Resolution provides no support for Opponent 02's already rejected objection under Article 53(a) EPC (see point (53) above), or for any further objection based upon some general duty to take into account the socio-economic effects of the grant of

patents in specific areas and to restrict the field of patentable subject-matter accordingly.

56. No arguments or evidence have been brought forward to the Board showing that the **publication or exploitation** of the claimed probes, vectors and cells is contrary to "ordre public" or morality. Furthermore, Rule 23e(2) EPC (cf point (44) above), which implements Article 53(a) EPC (see decision T 272/95, supra), does not exclude the subject-matter of claim 1 from patentability under Article 53(a) EPC.

57. The Board thus concludes that the subject-matter of claims 1 to 3 is not excluded from patentability under Article 53(a) EPC.

Referral of questions to the EBA (Article 112(2)(a) EPC)

58. Appellant II requested to refer the following questions to the EBA according to Article 112(1)(a) EPC:

"- In the case of patent applications which depend on donations of biological material of human origin in a critical way, is it necessary in view of Article 53(a) EPC that the previous informed consent of the donors of critical material is proven in the application proceedings by documents (or other means of proof)?

If the answer to the question is "yes":

- Should the previous informed consent in view of Article 53(a) EPC include an explicit consent to the commercial exploitation of the donations with the aid of patents?

and:

- Should the previous informed consent in view of Article 53(a) EPC include a benefit sharing agreement?"

59. The questions suggested by Appellant II do not concern the uniform application of the law, since this Board does not take a view of the law different to any earlier case.

Furthermore, when examining whether an important point of law arises which may justify the referral of the questions to the EBA, the Board observes that the EPC contains no provisions concerning a necessity on behalf of patent applicants or proprietors of providing any kind of proof about a previous informed consent in the proceedings before the EPO. When the legislator amended the Implementing Regulations of the EPC by adding Rules 23(b) to 23(e), it did not choose to introduce such provisions, in accordance with Recital (26) of the Directive, which in the context of previous informed consent makes reference to national law (cf point (48) above). The legal situation is thus considered to be clear in this regard, and the Board concludes that no important point of law arises.

Therefore, Appellant II's request for referral of questions to the EBA is refused.

Industrial applicability (Article 57 EPC) and Sufficiency of disclosure (Article 83 EPC)

60. Claim 1 of auxiliary request III refers to a nucleic acid probe defined by its nucleotide sequence.

According to Appellant II the possible uses of such probes were the cloning of BRCA1, the detection of BRCA1 or of mutations thereof in Southern blots and the detection of BRCA1 transcripts in Northern blots. These were not industrial applications in the sense of Article 57 EPC in connection with Rule 23e(3) EPC, which required that, with regard to inventions concerning the human body and its elements, the industrial application of a sequence or a partial sequence must be disclosed in the patent application.

The capacity of a single stranded DNA sequence to hybridize with a complementary single-stranded sequence was a consequence of the physico-chemical properties of each single-stranded DNA molecule and was thus a universal characteristic thereof. It could not have been the intention of the legislator to accept such universal characteristic as basis for an industrial application within the meaning of Article 57 and Rule 23e(3) EPC, as this would have the consequence that each and every single-stranded DNA was industrially applicable thereby depriving Rule 23e(3) EPC of any range of application.

61. Opponent 02, although referring to the requirements of Article 83 EPC, argued that the subject-matter of claim 1 did not meet the patentability requirements of the EPC, as it referred to a sequence for which no use

and no function was indicated which meant that it lacked any technical application.

62. It is not disputed between the parties that the patent in suit discloses that the present invention relates to the human breast cancer predisposing gene BRCA1, some alleles of which cause susceptibility to cancer, particularly breast and ovarian cancer (see paragraph [0017] of the patent in suit). In view of the provision of such a diagnostic target, a probe sequence specifically hybridizing to the BRCA1 gene, or as in the case of the probes according to claim 1 specifically hybridizing to the transcribed mRNA, is considered to be useful for diagnostic purposes. Therefore, the probes according to claim 1 do not only serve as research tools for the detection of complementary single stranded DNA molecules as argued by Appellant II, they also can be commercially applied for diagnostic purposes in order to detect the presence of BRCA1 allele predisposing an individual to cancer. The probes are explicitly disclosed in the patent as being useful in nucleic acid diagnosis and diagnostic kits (see paragraphs [0149], [0155] and [0156] of the patent in suit) and furthermore can be used to detect the length of a BRCA1 transcript and thereby detect larger deletions in the gene.

63. In the letter dated 18 January 2006, Appellant II argued, that the results obtainable by using the claimed probes at the relevant date were speculative and could not be considered to result in a specific, substantial and plausible diagnostic test. On pages 11 to 14 of said letter he referred to document D154 and

extensively cited contemporary statements ("zeitgenössische Aussagen").

64. These statements were made by a number of scientists who all were involved in research projects dealing with BRCA1. Although none of the statements contains an exact date, Appellant II considers all of them to date from autumn 1994. The statements draw a picture of the situation in the scientific community in 1994. They describe the aims and strategies of the different working groups, they express doubts and critics on the results of other groups and even refer to rivalries between specific groups. They do not, however, allow one to convincingly draw the conclusion, that the subject-matter of claim 1 of auxiliary request III lacks industrial applicability.

65. Appellant II has repeatedly referred to a decision of the Opposition Division published in the Official Journal of the EPO (2002, page 293), which concerned a patent application disclosing a list of speculative functions of a claimed protein. The Board notes however that the technical circumstances underlying this decision are different from the present ones, so that for this reason alone it can have no bearing on the present case.

66. The Board considers decision T 898/05 of 7 July 2006 to be relevant to the present case. It refers to the nucleotide sequence and the encoded amino acid sequence of the human transmembrane receptor Zcytor1, which is proposed for use in different screening methods for receptor ligands as well as for agonists and antagonists of the natural ligand. For the agonists as

well as for the antagonists several therapeutic applications are indicated. The Board when analysing the relevant case law of the Boards of Appeal with regard to the requirements of Article 57 EPC (cf Case Law of the Board of Appeal of the EPO, 5th Edition 2006, Chapter I.E.1), considers that this Article refers to the concepts of "financial (commercial) gain" (cf decision T 144/83, OJ EPO 1986, 301) and "profitable use" (cf decision T 870/04 of 11 May 2005). The Board came to the conclusion that these concepts were not to be understood in the narrow sense of an actual or potential profit or of a commercial interest, but rather they had to be "...understood in the wider sense that the invention claimed must have such a sound and concrete technical basis that the skilled person can recognize that its contribution to the art could lead to practical exploitation in industry."

The Board continued that it is necessary to disclose in definite technical terms the purpose of an invention and how it can be used in industrial practice to solve a given technical problem, this being the actual benefit or advantage of exploiting the invention. It was concluded that a product which is definitely described and plausibly shown to be usable, i.e. in the case of decision T 898/05 for curing a disease, might be considered to meet the requirements of Article 57 and Rule 23e(3) EPC (cf points (1) to (8) of the reasons for the decision).

67. This Board considers that the nucleic acid probes of claim 1 of auxiliary request III are definitely described and plausibly shown in the patent to be useful in the diagnosis of cancer, particularly breast

or ovarian cancer and finds itself therefore confronted with a technical situation corresponding to the one underlying decision T 898/05 which it considers to be based on a correct interpretation of the law.

Accordingly, the requirements of Article 57 and Rule 23e(3) EPC are met by the subject-matter of clams 1 to 3 of auxiliary request III.

68. Appellant II, in a letter dated 14 July 2007, has further requested to refer two question to the EBA pursuant to Article 112(1)(a) EPC. The Board notes that the first question concerned Appellant I's main request only, which was found by the Board not to meet the requirements of Article 123(2) EPC (see points (2) to (6) above). Thus, it is the second question that will be addressed in the present decision. It read as follows:

"Do sequences or partial sequences of a gene, the function of which is merely declared to be a probe, fulfil the requirement of industrial applicability according to Rule 23e(3) and Article 57 EPC?"

69. The question proposed by Appellant II (see point (68) above) does not relate to a uniform application of the law, as this Board does not take a view of the law different to earlier cases.

When examining whether an important point of law may justify the referral of the question to the EBA in accordance with Article 112(1) EPC, the Board notes that Rule 23e(3) EPC requires that the industrial application of a sequence must be disclosed **in the**

patent application. The same wording can be found in Article 5.3 and recital (22) of the Directive. The Board, having found that the **patent application** discloses an industrial application of the claimed nucleic acid probe, namely its use in diagnosis of cancer, considers Appellant II's question wherein it is assumed that the claimed sequence "is merely declared to be a probe", which, therefore, denies its use as a diagnostic tool, as being hypothetical and not relating to the facts of the present case. Such questions however, shall not be referred to the EBA (cf decision T 118/89 supra). Appellant II's request is therefore rejected.

70. The Board is moreover convinced in view of the above considerations that the patent contains sufficient information to allow a skilled person to make and technically apply the subject-matter of claims 1 to 3, so that, contrary to the argumentation brought forward by Opponent 02, the requirements of Article 83 EPC are met.

Right to priority (Articles 87 to 89 EPC)

71. The second priority document (P2) refers at page 6, lines 24 to 26 to "a probe consisting of nucleotide positions 3575 to 3874 of BRCA1" which was used for hybridization in a blot containing RNA from different tissues, and at page 24, lines 14 to 15 to the "coding sequence for a BRCA1 polypeptide is shown in SEQ ID NO: 1". The Board can follow Appellant I's argumentation that a skilled person would understand that the nucleotide positions mentioned on page 6 are the positions of SEQ ID NO: 1, since in the only other

nucleotide sequence disclosed in the second priority document (P2) being long enough, i.e. SEQ ID NO: 13, positions 3575 to 3874 lie in the intron (denoted in lower case letters). A skilled person would realize that it did not make sense to use an intron sequence to hybridize in a Northern blot to an RNA molecule from which the introns are spliced out.

Nucleotide positions 3575 to 3874 of SEQ ID NO: 1 of the second priority document (P2) have been shown by Appellant I to be identical to nucleotide positions 3631 to 3930 of SEQ ID NO: 1 of the application, which sequence is specified in claim 1. This has not been disputed by any of the other parties. Furthermore, page 27, line 21 explicitly refers to "probes comprising (...) polynucleotides of the present invention". Therefore, the Board considers that a nucleic acid probe comprising the DNA sequence specified in claim 1 is directly and unambiguously derivable from the second priority document (P2).

Moreover, the Board is convinced that a nucleic acid probe comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 35, 38, 41, 42, 47, 57, 62, 67, 72 and 81 is directly and unambiguously derivable from Table 9 on pages 73 and 74 of the second priority document.

The Board thus considers that the second priority is validly claimed for the subject-matter of claims 1 to 3.

Novelty (Article 54 EPC)

72. Opponents have argued that the YAC clone 22HE5 mentioned in Figure 2 of document D11 was prejudicial to the novelty of the subject-matter of claim 1. It had been shown by document D136 that this YAC clone contained exon 11 along with other exons of BRCA1, and the first sequence mentioned in claim 1 also related to exon 11.

73. The Board cannot follow this line of argument, since it has not actually been proven by document D136 or any other document on file that the YAC clone 22HE5 mentioned in document D11 contains any of the sequences specified in claim 1. According to the established case law of the Boards of Appeal (see e.g. decision T 464/94 of 21 May 1997), it is not appropriate to base a decision on the novelty of a claimed invention on considerations of likelihood. Rather, in order to revoke a patent for lack of novelty, the deciding body must be certain that based on the arguments and evidence submitted, the claimed subject-matter lacks novelty. In the absence of the required proof, the Board must thus conclude that the subject-matter of claim 1 is novel over document D11. In this respect, the Board concurs with the opinion expressed by the Opposition Division in the decision under appeal.

Inventive step (Article 56 EPC)

74. The closest prior art is considered to be represented by document D11 which discloses a physical map of the BRCA1 region on chromosome 17q12-21, said map comprising a contig of 137 overlapping YAC and P1

clones. The location of the BRCA1 gene is indicated to be proximal (centromeric) to the marker D17S78 and distal (telomeric) to the marker D17S776 (see Figure 2 of document D11).

74.1 Appellant I argued that considering document D11 as the closest prior art was based on hindsight and therefore inappropriate. As shown in Exhibit 22 submitted with letter of 24 July 2007, the prior art documents D52, D88, D10, D22, D112 and D122 had suggested chromosomal regions for BRCA1 different to that disclosed in document D11, and it only turned out later that the region for BRCA1 indicated in document D11 was correct.

74.2 The Board notes that documents D52, D88 and D10, which were published earlier than document D11, suggest regions for the BRCA1 gene that are larger in size but include the one suggested in document D11. As document D11 had already narrowed down the BRCA1 region, the Board considers that the skilled person would have preferred to start from this smaller region rather than from those regions suggested in documents D52, D88 and D10.

74.3 Document D22, which was published three months before document D11, suggests that the BRCA1 gene lies distal to the marker D17S702 and proximal to the marker EDH17B. The analyses of the results from "family 64" gave rise to the suggestion that the marker EDH17B could be the distal boundary for the BRCA1 gene (which information is in contradiction to that of document D11). At the end of document D22 a section "Note Added in Proof" states: "Subsequent analysis of the offspring of individual 309 in family 64 has indicated that the

ovarian cancer case did not inherit the putative linked haplotype. This suggests that either the ovarian cancer is a sporadic case or that the family is not linked to 17q12-21." The Board notes that in view of this statement, the skilled person would not have relied on the information that the marker EDH17B is the distal boundary, and would have given more weight to the information given in document D11.

74.4 Document D112, which was published more than a year before document D11, suggests a location for the breast-ovarian cancer locus between the markers D17S588 and D17S579. It is stated on page 742, first paragraph: "[I]n contrast, the recombination that places the cancer gene below D17S579 is evident only in woman 25. She developed breast cancer at age 57 years, an age significantly higher than the mean age at onset (41.5 years) of breast cancer in the family. None of her five daughters (ages between 20 and 37 years) is affected. If this case of breast cancer is sporadic, the recombinant has not mapping value". Because of this statement, the skilled person would have been reluctant to rely on the information concerning the marker D17S579. Since this information is furthermore in contradiction to that of document D11, the Board considers that the skilled person would not have started from document D112 as the closest prior art.

74.5 Document D122 provides information which, contrary to the other documents mentioned above, is not based on linkage studies with breast/ovarian cancer families, but on examination of sporadic breast cancers for deletions as measured by loss of heterozygosity. The smallest common region that was deleted occurred

between the markers D17S846 and D17S746. The document discusses possible reasons for an inconsistency with the results of another publication, one such reason being that "the locus we have defined may be relevant only in sporadic breast cancer and not in hereditary breast cancer" (page 2549, column 2, lines 4 to 6). The possibility of two separate loci on 17q12-21 important in breast cancer development, BRCA1 and a second locus defined by loss of heterozygosity, is also discussed in document D11 (see page 477, column 1, lines 36 to 44), as the region identified in the earlier document D122 does not overlap with that identified in document D11. Since the data of document D112 are not based on linkage studies with affected families, the Board considers that a skilled person would have given more weight to the information disclosed in document D11.

74.6 In view of these considerations, the Board concludes that while the correct chromosomal region including the BRCA1 gene was indeed in doubt at the second priority date, document D11 would have been selected by the skilled person as the most promising starting point.

75. Having regard to the closest prior art document D11, the technical problem to be solved is the provision of nucleic acid probes which are suitable to identify the BRCA1 gene.

The Board is satisfied that this problem has been solved by the nucleic acid probes according to claim 1. The probe with the sequence first mentioned in claim 1 has been shown to detect a single transcript in Northern blots (see Figure 7 of the patent in suit), and the sequences of SEQ ID NOs: 35, 38, 41, 42, 47,

57, 62, 66, 67, 72 and 81 consist of fragments of the BRCA1 gene (i.e. SEQ ID NO: 1) representing intron/exon junctions (see Table 9 of the patent in suit), which are likewise suitable to detect the BRCA1 gene.

76. In order to be able to provide nucleic acid probes suitable to detect the BRCA1 gene, a skilled person starting from the disclosure of document D11 would first have to identify the BRCA1 gene and isolate (at least part of) its sequence. The key question is therefore whether at the second priority date, a skilled person would have reasonably expected to be able to identify and isolate the BRCA1 gene.

77. A number of decisions of the Boards of Appeal in the technical field of biotechnology have pointed out that, in evaluating the attitude of the skilled person, one should not confuse the "hope to succeed", which is linked to the wish that a result be achieved, with the "reasonable expectation of success", which is linked to the ability to reasonably predict, based on the particular technical circumstances, a successful conclusion of the project within acceptable time limits (see decisions T 296/93, OJ EPO 1995, 627, T 923/92, OJ EPO 1996, 564, and T 223/96 of 29 January 1999). In this respect, each case has to be assessed on its own merits, and any hindsight has to be avoided.

78. It is evident that the skilled person, departing from the disclosure of document D11, would have readily undertaken to identify the BRCA1 gene in the hope to succeed. The question remains, however, whether, when evaluating realistically the chances of success at the

second priority date, he or she would have had a reasonable expectation of achieving the desired result.

79. For the reasons given hereinafter, the Board found the arguments concerning this question as put forward by Appellant I more convincing than those put forward by Appellant II and the remaining Opponents.

79.1 In order to identify the BRCA1 gene, for which no information about its protein product was available at the relevant priority date, a skilled person would have been aware that a positional cloning approach had to be applied. As a first step in such an approach, polymorphic markers are identified by linkage analysis using DNA of well-documented families (kindreds) with inherited cases of the disease in question (here: breast cancer), in order to narrow the putative chromosomal region containing the gene to a manageable size of about 600 kb (see for instance documents D120 and D125).

79.2 In the present case, the closest prior art document D11 had already narrowed the relevant chromosomal region down to approximately 1.5 Megabases (Mb) and provided a physical map of this region. Although this region was the most promising starting point, there was however no certainty that it did indeed contain the BRCA1 gene (see points (74.1) to (74.6) above). A skilled person would have been well aware that any cloning efforts starting from the wrong chromosomal region would evidently result in ultimate failure.

79.3 Furthermore, there was no certainty that suitable polymorphic markers could indeed be identified in order to further narrow down the relevant chromosomal region. In order to be successful, it would not only be necessary to find polymorphic markers that map to the region, but also to have well-documented kindreds with cases of inherited breast cancer at hand, which would need to contain individuals with recombination events located such that they would provide the necessary mapping information. Apart from the substantial amount of experimentation involved in the linkage analysis, success thus required a substantial amount of luck which a skilled person could not reasonably predict.

79.4 If refining the chromosomal region containing the BRCA1 gene to a sufficiently small size would have been successful, the next steps would be to identify gene sequences within that chromosomal region and to look for a gene which contains a causal mutation, i.e. a mutation existing within that gene which is found to co-segregate with breast cancer in a statistically significant manner, but not with control or non-cancer patients. Finding such a mutation would not only involve substantial amounts of work, but would also require a "lucky strike", which could in no way be predicted even if well-documented breast cancer kindreds were available.

80. Considering the uncertainties of the project as outlined above, the Board concludes that at the second priority date, a person skilled in the art would not have reasonably expected to successfully arrive at the cloning of the BRCA1 gene within acceptable time limits merely by way of routine experimentation. The Board is

convinced that solving the technical problem was a major breakthrough which was not obvious to the skilled person.

81. The Opponents have argued that the claimed subject-matter was obvious to the skilled person because document D11 referred to sequence information relating to clone extremities which were available from GenBank and directly from the authors. One of these sequences had the accession number L18209 and contained a CpG island, as was evidenced by document D31, which corresponded to the promoter region of the BRCA1 gene. It would thus have lead the skilled person to the identification of the BRCA1 gene.

In this regard, the Board considers that the Opponents have not sufficiently proven if or what information on the sequence termed L18209 was available to the public at the second priority date. Document D31 is a print-out of a database entry which carries the date 10 October 1995, and cannot thus constitute evidence as to what was available to the public on 2 September 1994, the second priority date. Document D11 itself neither mentions the term "L18209", nor does it provide information about its sequence. For these reasons the argumentation based on sequence L18209 must fail.

82. Opponents have also argued that in order to further narrow down the BRCA1 region identified in document D11 to a size of approximately 650 kb, the marker D17S1141, also known as UM44_, would have been available to the skilled person. This would then have easily led to the identification of the BRCA1 coding region. Document D128, a print-out of the gdb database, disclosed this

marker as having been available from Dr Chamberlain as of 18 February 1994. Documents D159 and D160, also print-outs of database entries, provided additional evidence that the marker was publicly available. The post-published document D129 described the marker in detail.

Concerning the question whether a disclosure available from the internet, like for example the database entry of document D128, is part of the state of the art under Article 54(2) EPC, a strict standard of proof is to be applied (see decision T 1134/06 of 16 January 2007). In the present case, the Board does however not consider it necessary to investigate the question whether document D128 was indeed available to the public at the second priority date, because even if it was, the Board could not follow Opponents' line of argument that the claimed subject-matter lacked an inventive step under Article 56 EPC. The reason for this is that the skilled person would not have known from the supposed disclosure of document D128 that the marker D17S1141 was suitable to narrow down the approximately 1.5 Mb BRCA1 region as identified in document D11. This fact only became known to the skilled person after the second priority date. As pointed out in numerous decisions by the Boards of Appeal, any *ex post facto* analysis has to be strictly avoided in the assessment of inventive step (see Case Law of the Boards of Appeal of the European Patent Office, 5th edition 2006, chapter I.D.5.).

83. For these reasons, the subject-matter of claim 1 is considered to involve an inventive step. Since claim 2 relates to a replicative cloning vector comprising a

DNA according to claim 1, and since claim 3 relates to a host cell transformed with a vector of claim 2, the Board likewise considers the subject-matter of claims 2 and 3 to involve an inventive step.

84. In view of the above, the claims of auxiliary request III are allowable.

Order

For these reasons it is decided that:

The appeals are dismissed.

The Registrar: The Chair:

P. Cremona U. Kinkeldey