BL O/304/12

06 August 2012

PATENTS ACT 1977

BETWEEN

Berni Hambleton of Sterling IP	Claimant
and	
Cold Spring Harbor Laboratory	Defendant

PROCEEDINGS

Application under section 72 of the Patents Act 1977 for revocation of patent EP(UK) 0665886B1

HEARING OFFICER Peter Slater

DECISION

Background

1 EP0665886B1 ("the patent") entitled "*Cyclin complex rearrangement and uses related thereto*" was filed 18 October 1993 in the name of Cold Spring Harbor Laboratory ("the defendant"). The patent claims priority from two earlier US applications 07/963,308 ("P1") and 07/991,997 ("P2") filed on 16 October 1992 and 17 December 1992 respectively. The patent was granted on 11 June 2003.

2 An application under section 72(1)(a) of the Patents Act 1977 for revocation of the patent was filed by Berni Hambleton of Sterling IP ("the claimant") on 31 December 2010. The application was accompanied by a statement of grounds alleging that the invention as claimed lacks an inventive step. The application follows an earlier request by the claimant for an opinion under section 74(A) of the Act in relation to the validity of the patent which was issued on 17 November 2010 (Opinion Number 13/10).

3 The defendants filed their counterstatement on 28 April 2011, and a hearing date was set for 9 February 2012. The claimants filed evidence-in-chief on 29 August 2011, and the defendants filed their evidence on 10 October 2011. The claimants took the opportunity to file evidence-in-reply on 22 November 2011.

4 Following a preliminary decision on the admissibility of the claimants evidence-in-reply dated 15 March 2012, the defendants were given a further opportunity to file

additional submissions which they did on 12 April 2012. Both sides have declined the opportunity to be heard and have instead opted for a decision on the papers.

The patent

5 The patent provides a method of identifying a transformed or abnormally proliferating cell by determining the subunit composition of a complex that includes D-type cyclins and comparing it to the equivalent complex in normal cells. In normal cells, a quaternary complex of cyclin-dependent kinases (CDK), proliferating cell nuclear antigen (PCNA) and p21 is formed, but in transformed cells this complex is disrupted and the CDK becomes associated with a protein p16 whilst the cyclin is associated with another protein p19. The patent includes claims to the purified and/or recombinant polypeptide known as *p16* (including the amino nucleic acid sequences thereof) and to antibodies to the proteins, and associated diagnostic test kits for use in the identification and treatment of cancer.

6 The patent comprises 6 independent claims, 1, 10, 19, 21, 32 & 34. However the relevant claims under consideration in this decision are claims 1, 21 to 25 and 34 which read as follows:

> *1. A method of identifying a transformed or abnormally proliferating cell, comprising:*
>
> *(A) determining, in a test cell(s), the subunit composition of a complex comprising a protein having a molecular weight of about 16 kDA, 19 kDA or 21 kDa and either a cyclin dependent kinase (Cdk), a cyclin, or both a cdk and a cyclin, wherein the protein is predominantly a protein having an apparent molecular weight of about 21KDa in a normal cell, or is predominantly a protein having an apparent molecular weight of about 19KDa or about 16KDa in a transformed or abnormally proliferating cell, and*
>
> *(B) comparing the subunit composition of step (A) with the subunit composition of a like complex found in a normal cell, wherein an alteration in the subunit composition is indicative of transformation or abnormal proliferation of the test cell.*
>
> *21. A diagnostic kit for identifying transformed cells comprising:*
>
> *(a) a nucleic acid probe (sense or antisense) which specifically hybridises to the nucleic acid sequence of SEQ ID No 3 and selectively detects a nucleic acid encoding a 16kDa protein which binds to cyclin dependent kinase 4 (cdk4), which probe is for measuring, in a sample of cells isolated from a patient, the presence or absence of a nucleic acid encoding said 16kDa protein; and/or*
>
> *(b) an antibody specific for the 16kDa protein for measuring, in a sample of cells isolated from a patient, an amount of said protein.*
>
> *22. A kit according to claim 21 wherein the antibody is specific for said polypeptide which has an amino acid sequence of SEQ ID No 4.*

23. The nucleic acid of any of claims 16-20 or the kit of claims 21 or 22, wherein the nucleic acid, the probe or the antibody is labelled with a detectable label selected from the group consisting of: an enzyme, an enzyme substrate, a coenzyme, an enzyme inhibitor, a fluorescent marker, a chromophore, a luminescent marker, a specifically bindable ligand and a radioisotope.

24. the nucleic acid or the kit of any of claims 19 to 21 or 23, wherein the nucleic acid or probe hybridizes to an mRNA transcript encoding said protein.

25. the nucleic acid or kit of any of claims 16 to 21 or 23, wherein the nucleic acid or probe is approximately 75 to 150 nucleotides in length.

34. An antibody which is specifically immunoreactive with the protein of SEQ ID No 4

The Law

7 The Comptroller's powers to revoke a patent on the application of another person are set out in section 72(1) of the Patents Act 1977. This reads in part as follows:

72 (1) Subject to the following provisions of the Act, the court or the comptroller may on the application of any person by order revoke a patent for an invention on (but only on) any of the following grounds, that is to say-

(a) the invention is not a patentable invention;

(b)…

(c) the specification of the patent does not disclose the invention clearly enough and completely enough for it to be performed by a person skilled in the art.

8 Further to section 72(1)(a) above, I must also look to section 1(1) which defines the requirements for a patentable invention, namely that:

1.-(1) A patent may be granted only for an invention in respect of which the followingconditions are satisfied, that is to say –

(a) the invention is new;

(b) it involves an inventive step;

(c) …

9 Section 2(2) sets out what is to be considered the state of the art:

(2) The state of the art in the case of an invention shall be taken to comprise all matter (whether a product, a process, information about either, or anything else) which has at any time before the priority date of that invention been made available to the public (whether in the United Kingdom or elsewhere) by written or oral description, by use or in any other way.

10 Section 3 sets out how the presence of an inventive step is determined:

3. An invention shall be taken to involve an inventive step if it is not obvious to a person skilled in the art, having regard to any matter which forms part of the state of the art by virtue only of section 2(2) above (and disregarding section 2(3) above).

11 Also especially relevant is section 5 which sets out the requirements for determining the priority date of an application for a patent:

> *5.-(1) For the purposes of this Act the priority date of an invention to which an application for a patent relates and also of any matter (whether or not the same as the invention) contained in any such application is, except as provided by the following provisions of this Act, the date of filing the application.*
>
> *(2) If in or in connection with an application for a patent (the application in suit) a declaration is made, whether by the applicant or any predecessor in title of his, complying with the relevant requirements of rules and specifying one or more earlier relevant applications for the purposes of this section made by the applicant or a predecessor in title of his and the application in suit has a date of filing during the period allowed under subsection (2A)(a) or (b) below, then -*
>
> > *(a) if an invention to which the application in suit relates is supported by matter disclosed in the earlier relevant application or applications, the priority date of that invention shall instead of being the date of filing the application in suit be the date of filing the relevant application in which that matter was disclosed, or, if it was disclosed in more than one relevant application, the earliest of them;*
> >
> > *(b) the priority date of any matter contained in the application in suit which was also disclosed in the earlier relevant application or applications shall be the date of filing the relevant application in which that matter was disclosed or, if it was disclosed in more than one relevant application, the earliest of them*

Grounds for revocation

12 The claimants allege that the invention as defined in claims 1, 21 to 25 and 34 is not entitled to either of the priority dates of 16 October 1992 or 17 December 1992 arising from the earlier US applications 07/963,308 ("P1") and 07/991,997 ("P2") respectively, and that the invention therefore lacks an inventive step over the disclosure in:

D1: *Genes & Development*; Vol 7, pp 1572-1583 (1993). Xiong *et al.* "*Subunit rearrangement of the cyclin-dependent kinases is associated with cellular transformation*"

13 The claimant relies on a second document to demonstrate what was known at the priority date of the invention, namely:

D2: *Antibodies: a laboratory manual; Harlow & Lane (1988). Cold Spring Harbour Press*

14 The claimant's arguments are substantially the same as those raised in their original request for an opinion. They begin by considering claims 21, 22 and 34. They allege that claims 21 and 22 relate to a kit comprising an antibody which is specifically immunoreactive with protein SEQ ID No. 4 (the sequence for p16) and that claim 34 relates to the associated antibody. They identify the underlying inventive concept therefore to be "antibodies against p16". They argue that "*although antibodies are not disclosed in D1, producing them would have been an obvious step for the skilled person to make. Generating an antibody to a known antigen has been common general knowledge since at least 1975 (the discovery of monoclonal antibodies)".*

15 The claimant further extends their arguments to claim 1, which they also consider to be obvious in the light of the disclosure in D1, although they identify the inventive concept of this claim slightly differently to that of the other claims, as being "*determining the subunit composition of a complex comprising a p16, p19, or p21 protein*."

16 The defendants maintain that the invention is entitled to the priority date of 17 December 1992 arising from US application 07/991,997 and that therefore D1, does not form part of the state of the art.

17 The claimant's arguments are laid out in some detail in their statement of grounds filed on 31 December 2010, and a further letter dated 22 November 2011 accompanying their evidence-in-reply. I do not intend to repeat those arguments here but will pick up on relevant points as they arise.

18 Both parties have made reference to the European Patent Office ("EPO") examination report, and the opinions expressed therein by the EPO's examiner. The defendants in particular have emphasised the conclusions reached by the examiner in respect of the priority date and inventive step. However, I have not considered this in any great detail, as I am not bound by the view of the EPO's examiners, and I think it more appropriate to consider the issues being raised with a fresh pair of eyes.

19 Furthermore, I have not considered the comments made by the claimant in respect of the prosecution of the corresponding US application US5889169, as I think these are irrelevant given that the content and the claims of the two applications are different.

20 The claimants have also referred to a number of other judgments and Office decisions, particularly in the covering letter accompanying their evidence-in-chief which I have not considered in any detail particularly where they have failed to elaborate on their significance, for example, *Mayflower Products Application (BL 0/129/86)* and *Rhone-Poulenc Agrochimie's Patent (BL 0/20/94)*.

Establishing the priority date

21 It is clear that before considering inventive step, I must first determine whether the invention as claimed is entitled to its earliest priority date and hence whether D1 forms part of the state of the art.

22 It is well established practice, that in order for a claimed invention to be entitled to priority from an earlier application, it must, in the words of section 5(2)(a) of the 1977 Act, be *"supported by matter disclosed"* in that earlier application. Article 87(1) of the European Patent Convention expresses the requirement as being that priority can only be accorded in respect of *"the same invention*" as one in the earlier application. Section 5 is one of the sections which is declared to be intended to have the same effect as the corresponding provision of the EPC: see section 130(7) .

23 In case *G2/98*[1] the Enlarged Board of Appeal of the European Patent Office equated "the same invention" in Article 87(1) with "the same subject-matter" in Article 87(4). It expressed the requirement for claiming priority as follows:

> *"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."*

24 The Court of Appeal explained this requirement in *Unilin Beheer NV v Berry Floor NV*[2] at paragraph 48 as follows:

> *"The approach is not formulaic: priority is a question about technical disclosure, explicit or implicit. Is there enough in the priority document to give the skilled man essentially the same information as forms the subject-matter of the claim and enables him to work the invention in accordance with that claim?"*

25 As Kitchin J observed in *Abbott Laboratories Ltd v Evysio Medical Devices plc*[3] at paragraph 228, after citing *G2/98* and *Unilin v Berry* :

> *"So the important thing is not the consistory clause or the claims of the priority document but whether the disclosure as a whole is enabling and effectively gives the skilled person what is in the claim whose priority is in question. I would add that it must "give" it directly and unambiguously. It is not sufficient that it may be an obvious development of what is disclosed."*

26 In other words, I will need to assess whether the inventive concept at the heart of the invention as claimed is disclosed in either one of the US priority documents P1 or P2. I must decide whether, the disclosure in either of these documents as a whole is enabling and effectively gives the skilled person, in possession of the common general knowledge, what is in the claim whose priority is in question. Furthermore, the skilled person must be able to derive the subject-matter of the claim directly and unambiguously from the disclosure in the priority document, it is not sufficient that it may be an obvious development of what is disclosed.

27 I have noted the claimants comments in respect of whether or not a valid claim to priority can be made if the priority document is silent as to the presence of an essential feature, and in particular their references to the CIPA Guide to the Patents Act, section 5, page 184 as follows:

> *"It would therefore appear to follow that priority cannot be accorded from a priority document which is wholly silent as to an essential feature of the eventually claimed subject matter."*

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[1] G2/98 [2001] OJEPO 413 , [2002] EPOR 167
[2] Unilin Beheer NV v Berry Floor NV [2004] EWCA Civ 1021, [2005] FSR 6
[3] Abbott Laboratories Ltd v Evysio Medical Devices plc [2008] EWHC 800 (Pat), [2008] RPC 23

28 Furthermore, I have taken note of their references to paragraphs 5.23 and 6.03 of the manual of patent practice. However, I think it is still appropriate to follow the practice as laid out in paragraphs 22 to 26 above.

29 First of all, I will consider the identity of the skilled man and the common general knowledge at the priority date.

The skilled person

30 A patent specification is addressed to those likely to have a practical interest in the subject matter of the invention, and such persons are those with practical knowledge and experience of the kind of work in which the invention is intended to be used. The addressee comes to a reading of the specification with the common general knowledge of persons skilled in the relevant art, and he or she reads it knowing that its purpose is to describe and demarcate an invention. The skilled person is unimaginative and has no inventive capacity. In an appropriate case the patent may be addressed to a team of persons with different skills.

31 There is common ground here. Both parties appear to agree that the person skilled in the art is an individual or group of people working in protein biochemistry research, probably with at least a PhD and possibly several years postdoctoral experience. Such a person would routinely carry out standard methods such as protein extraction, antibody generation, purification and protein sequencing.

Common general knowledge

32 The law as to what constitutes common general knowledge is set out in the decisions of the Court of Appeal in *General Tire & Rubber Co v Firestone Tyre & Rubber Co Ltd*[4] at paragraphs 482-483 and *Beloit Technologies Inc v Valmet Paper Machinery Inc*[5] at paragraphs 494-495. Counsel for the Patentees emphasised that, in order to constitute common general knowledge, it is not enough that information is generally known to the relevant skilled persons: it must also be, in the words of the Court of Appeal in *General Tire*, “generally regarded as a good basis for further action”. Laddie J put the same idea in slightly different words in *Raychem Corp's Patents*[6] at paragraph 40 when he said “generally regarded as sufficiently reliable to use a foundation for further work”.

33 Again there appears to be common ground here. Both parties agree that the relevant common general knowledge of the skilled person would include common laboratory techniques in addition to those techniques that are specifically used in protein biochemistry, and that document D2 is representative of the types of techniques that would have been routinely employed before the priority date. In essence, they agree that D2 represents the state of common general knowledge before the earliest relevant date of the patent in suit.

[4] General Tire & Rubber Co v Firestone Tyre & Rubber Co Ltd [1972] RPC 457
[5] Beloit Technologies Inc v Valmet Paper Machinery Inc [1997] RPC 489
[6] Raychem Corp's Patents [1998] RPC 31

34 Having identified the skilled person and the common general knowledge at the time, I will now move on to consider the invention as claimed, beginning with the so-called "antibody claims", claims 21, 22 and 34 (including claims 23 to 25).

The antibody claims

35 The question to ask here is do either of the priority documents P1 or P2 provide an explicit or implicit enabling disclosure of antibodies specific for p16 from which the skilled person could derive the subject matter of claims 21, 22 and 34.

36 The first of these documents, P1 relates to D type cyclins and complexes with p21 protein. There is no disclosure at all of p16 proteins within this document, and therefore there is no disclosure of antibodies against these proteins. Consequently the subject matter contained within claims 21, 22, and 34 of the patent is not entitled to the priority date of 16 October 1992 arising from document P1. Similarly claim 1, at least in as far as it relates to the p16 protein is not entitled to priority from this document either.

37 The second of these documents, P2, discloses an interaction between CDK4 and p16 in virus-transformed cells. This interaction is demonstrated in ^{35}S-Methionine labelled cell lysates immunoprecipitated with an antibody against CDK4, and separated using a polyacrylamide gel. This results in a 16kDa band in the polyacrylamide gel (see Figures 2 and 3 of the document). In addition to this, the document at page 7 states that the invention provides methods to diagnose the transformation of a cell using an antibody that recognises the interaction between p16 and CDK4; this is mirrored in claim 4, with claim 5 adding that antibodies are used to determine whether p16 is complexed.

38 Consequently, I consider that document P2 does not explicitly disclose antibodies against p16, it merely discloses that the p16 protein has been identified and isolated, although no sequence information about the protein is provided. This is entirely consistent with the view of the examiner in opinion 13/10 and the expert witness statement of Dr Brown submitted by the claimant with their letter of 29 August 2011.

39 I think it also useful here to consider the witness statement of Dr Brown, the claimant's expert witness, in slightly more detail.

Expert witness

40 The claimants in their evidence dated 29 August 2011 presented a statement on behalf of Dr Derek Brown, Director of Cheylard Biosciences who has significant experience in the field of biosciences including many years experience in generating, screening and characterising monoclonal antibodies.

41 In his witness statement Dr Brown makes clear that he was asked to review the granted patent and the priority documents in relation to claims 21, 22 and 34 of the patent in respect of antibodies that are specific for 16 kDa protein (p16) or the amino acid sequence SEQ ID. No. 4 (which is identified in the patent as representing the amino acid sequence of p16). Such specific antibodies he considered to be an

antibody that essentially does not cross-react with another protein or polypeptide apart from the one it has been raised against. Dr Brown was further asked by the claimant to assess the two US priority documents for any disclosure of the 16 kDa protein in these documents. He found that whilst there was no disclosure of this protein in the first priority document it was to be found in the second priority document. In his opinion, the first priority document did neither disclose antibodies against the 16 kDa protein nor the polypeptide of the sequence shown in SEQ ID No: 4. Dr Brown also considered that the second priority document 07/991,997 did not provide an explicit disclose of such antibodies, although it could be considered to disclose antibodies against complexes with p16 and a cyclin dependent kinase (CDK).

42 Finally, Dr Brown expressed the view that it would have been possible at the filing date of the patent 18 October 1993, and indeed was routine, to generate antibodies to an unsequenced protein that has been isolated on a gel.

43 Furthermore, the claimant argues that there is no implicit disclosure, in P2, of antibodies to the p16 protein. In their statement of 23 December 2010, they assert that P2 makes only a generic disclosure in relation to antibodies, and that this is only in respect of antibodies to the p16-CDK4 complex only. They conclude that antibodies to the specific p16 protein are not explicitly or implicitly disclosed, and that the requirements laid down by the EPO Enlarged Board of Appeal in G2/98 which states that a priority claim is only valid if the skilled person can derive the subject matter of the claim of the application in suit "directly and unambiguously, using common general knowledge, from the previous application as a whole...", have not been met as there is no direct and unambiguous disclosure of anti-p16 antibodies in P2.

44 The apparently limited nature of the disclosure In P2 is also suggested by Dr Brown in his witness statement at paragraphs 24 to 27. Dr Brown particularly refers to certain passages of P2 in making this assessment, including page 22, lines 15 to 30, although he only quotes from lines 15 to 22. I set out the entire passage below:

> *"For example, an agent can be developed that recognises the interactions between CDKs, cyclins, PCNA and low molecular weight polypeptides (such as p21, p19 and p16). The agent can then be contacted with the sample of cells for which transformation state is to be tested; presence of particular subunits in a complex will be indicative of transformation. For example, a CDK4-p16 complex will be indicative of transformation, as will a cyclin A-p19 complex.* ***Alternatively, agents which recognize different subunits can be used in conjunction, to determine the presence of interactions among the subunits. For example, an agent which recognizes p21 can be used in conjunction with an agent which recognizes a cyclin or a cyclin kinase, to determine whether p21 is complexed with either the cyclin or the cyclin kinase."*** [emphasis added]

45 The passage on page 7 of P2 also states that antibodies that can recognise the interaction between CDK4 and p16 could be used to detect transformation, and claim 5 states that an antibody can be used to determine whether p16 is complexed with CDK4. I therefore believe that the emphasised passage on page 22 (highlighted above) when considered in conjunction with the general teaching of P2, as set out on page 7 as well as in claim 5, means that P2 as a whole disclosed the invention of p16 antibodies. The document as a whole makes clear that antibodies against individual components of the complex, that is to say agents that recognise a

specific protein, are taught by P2. Whilst p21 is referred to as an example, given that the document discusses both p21 and p16, as well as p19 in essentially the same manner with independent claims for each of these proteins that take essentially the same form, the applicant therefore clearly considered that antibodies against p16 could be developed once the existence of the protein and its relevance to identifying transformed cells was established. In this respect, I believe that P2 provides an implicit disclosure of antibodies specific for p16. I note that this is entirely consistent with the view of the examiner in opinion 13/10 where at paragraph 18 the examiner states that:

> *"18. The passage on page 7 of document '997 states that antibodies that can recognise the interaction between CDK4 and p16 could be used to detect transformation, and claim 5 states that an antibody can be used to determine whether p16 is complexed with CDK4. However, the specification does not disclose antibodies specific for p16; the association between CDK4 and p16 is detected by co-immunoprecipitation with an anti-CDK4 antibody. Nevertheless, a skilled person reading the passage on page 7, and claim 5 would understand them to include antibodies specific for p16, not least because these antibodies would be a means to target p16-CDK4 complexes and exclude other CDK4 complexes in the cell. Therefore, antibodies specific for p16 are in my opinion implicitly disclosed in document '997"*

46 Is this implicit disclosure sufficiently enabling? I think it is. Again, I note the examiner's view in opinion 13/10 at paragraphs 19 to 21 below:

> *"19. The requester has provided a copy of a laboratory manual (D2) as indicative of the common general knowledge in the art at the priority date of the patent. In particular the requester has referred to chapter 5 of D2 as demonstrating that the generation of antibodies from a known protein was routine at the filing and priority date of the patent. Amongst the techniques disclosed in chapter 5 is the purification of radiolabelled antigens from polyacrylamide gels; the protein bands of interest are excised from the gel and the protein-containing band can either be injected directly into large laboratory animals, or the protein can be eluted from the excised band for immunisation of smaller laboratory animals. Thus it is clear that crude protein identification as a mere band on a gel was sufficient in order to raise antibodies against that protein at the priority date of the patent, and a skilled person would be well aware of this.*
>
> *20. The contents of D2 demonstrate what was known in the art at the time of filing of the patent. Specifically, it demonstrates that antibodies can be raised against protein bands excised from a polyacrylamide gel; these are protein bands such as those demonstrating the presence of the p16 protein in co-immunoprecipitates in figures 2 and 3 of document '997. In addition, the requester also points out (albeit in the argument for obviousness) that it was "not necessary that the protein be sequenced in order for it to be useful in the generation of antibodies. Rather once a protein was isolated in a band on a gel it could be cut out of the gel and recovered for immunisation…". The requester goes on to state that the generation of antibodies from a known protein was routine.*
>
> *21. Given what was known in the art at the time of filing of document '997, a skilled person reading this document would be capable of isolating the p16 band from the gels, and using the gel fragments or proteins eluted from these gels to immunise laboratory animals. Therefore, in my opinion, document '997 does provide an enabling disclosure of anti-p16 antibodies, and as the applicants are the first to identify the CDK4-p16 complex, they are also justified in claiming them in the patent."*

47 Having considered all the evidence before me, I can see nothing in the claimant's submissions to suggest the examiner's original opinion was incorrect. I believe the disclosure in the second US priority document 07/991,997 ("P2") to provide, albeit an implicit disclosure of antibodies for p16, one which is sufficiently enabling for a skilled person to derive the subject-matter of the invention as claimed in claims 21 to 25 and

34 directly and unambiguously from the disclosure in the priority document. I am also satisfied that the implicit disclosure in the priority document in light of the common general knowledge is sufficient to understand that these antibodies are not merely obvious but are clearly taught.

48 I realise that despite the disclosure in P2, a considerable amount of work on the part of the skilled person would still have been required to actually produce the antibodies against p16. The techniques available to the skilled person although well established are still not straightforward and would require a degree of effort to generate the desired antibodies. However, as the decision in *Biogen/Human beta-interferon*[7] makes clear, an enabling disclosure is made even if significant work was required to achieve the invention of the later application because this work would have been feasible given the existing state of the art. Therefore, I remain of the opinion that the disclosure in P2 is sufficient, given the state of the art and common general knowledge that I have identified, which could be applied once any protein had been identified and isolated in some form.

49 Consequently, I believe the invention as defined in claims 21 to 25 and 34 to be entitled to the priority date of 17 December 1992 arising from US application 07/991,997.

The invention as defined in Claim 1

50 The request for revocation was also made in respect of claim 1 of the patent, which as identified above is directed to subject matter of slightly different scope being directed in an inventive concept that is, as the claimant has identified essentially :

> *"determining the subunit composition of a complex comprising a p16, p19, or p21 protein"*

51 The claimants argue that the above wording is not found in either of P1 or P2. Instead, the wording "recognises the interaction between p16 and CDK4" is found. The concept of recognising an interaction between p16 and CDK4 is **NOT** the same as the concept behind determining the subunit complex comprising p16, p19 or p21 protein because for the latter specific tools are required, such as antibodies which specifically recognise the subunit. In contrast, recognition of the interactions with p16 and CDK4 can be performed on the mass of the complex or simply running the complex on a gel. Hence, the invention as defined in claim 1 is not entitled to the priority date of either P1 or P2.

52 However, I do not find the disclosure in P2, to be limited as the claimants suggest, to the concept of recognising an interaction between p16 and CDK4. As set out above the priority document makes clear at for example page 22, that the invention of the application can be wide ranging but revolves around the identification of the p16 protein as well as the p19 and p21proteins. Although only certain interactions are explicitly disclosed the document makes clear that many other complexes are contemplated or considered including a variety of complexes with p16 and that assaying these would be useful indicators as to whether a cell is transformed or not. The passage at page 22 of P2 makes clear that agents which recognise specific

[7] *Biogen/Human beta-interferon* [1999] EPOR 451 (T207/94)

subunits of the complexes formed, can be used to determine the presence of interactions between the subunits, and claim 4 of this document is not simply restricted to identifying a p16-CDK4 interaction, but more generally to interactions between p16 and cyclin dependent kinases.

53 Given the explicit and implicit disclosures I have identified above, and the teaching of this document regarding the methods of identifying p16 interactions which are not simply restricted to interactions with CDK4, I consider the invention as defined in claim 1 to be entitled to the same priority date as that of claims 21 to 25 and 34, namely that of 17 December 1992 derived from the second US priority document 07/991,997.

54 I therefore conclude that all of the claims that are the subject of this action i.e. claims 1, 21 to 25 and 34 are entitled to the priority date of 17 December 1992.

Inventive step

55 Having found all of the claims to be entitled to the priority date of 17 December 1992, and since D1 is a journal article published after this date, I conclude that D1 does not form part of the state of the art by virtue of Section 2(2) of the Act. The issue of whether the claims involve an inventive step over D1 is therefore a moot one which I do not have to consider here.

Conclusion

56 The invention as defined in claims 1, 21 to 25 and 34 of the patent is entitled to its priority date of 17 December 1992 and I can see no grounds to suggest that the patent is invalid for inventive step, as D1 does not therefore form part of the state of the art. The action is therefore dismissed as I can see no reason for the patent to be revoked.

Appeal

57 Under the Practice Direction to Part 52 of the Civil Procedure Rules, any appeal must be lodged within 28 days.

P R SLATER
Deputy Director acting for the Comptroller