BL O/221/13

28 May 2013

PATENTS ACT 1977

APPLICANT Agency for Science, Technology and Research

ISSUE Whether patent application GB1003527.7 complies with section 14(5)(c) and section 76(2)

HEARING OFFICER Dr Jim Houlihan

DECISION

1 The application is entitled "VHZ for diagnosis and treatment of cancer". It derives from a PCT application, PCT/SG2008/000294, which has a priority date of 10 August 2007 and was filed on 8 August 2008. It was published on 19 February 2009 as WO2009/022988 and republished in the national phase in the UK as GB2465907 on 9 June 2010.

2 The examiner had maintained his objection in three rounds of correspondence that the main claim is not supported, as required by section 14(5)(c) of the Act. In responding to the examiner's objections the applicant had amended the main claim which attracted an additional objection of added matter (section 76(2)).

3 At the first stage of the examination proceedings the examiner had raised an objection on the grounds of novelty and obviousness, by proxy, referring to the International Preliminary Examination Report on Patentability which was produced on 16 February 2010 when the application was in the international phase. As a result of amendment and the applicant's argument, the examiner did not pursue the novelty and obviousness objections and therefore I do not need to deal with those issues here.

4 The matter came before me at a hearing which therefore concerned two questions: (i) whether claim 1 contained added matter and (ii) whether this claim and its dependent claims, 2-8, are supported by the description.

5 The applicant was represented by Mr Richard Clegg of Mewburn Ellis who was assisted by Ms Elizabeth Ruszala and Mr Thomas Walker. The examiner, Dr Jeremy Kaye, also attended. The hearing took place by videoconference on 3 April 2013.

6 The examiner had produced a pre-hearing report dated 28 March 2013 which responded to the points in the agent's final letter of 21 March. No skeleton arguments were filed by the agent before the hearing.

7 In the preliminary stages of the hearing Mr Clegg noted that the two month as-of-right extension to the compliance period, requested on 8 February, expired on 8 April 2013. Accordingly, he indicated that he would file a request for a discretionary extension for a further two months before this deadline. This is to cover the possibility that if I found in the applicant's favour there needs to be time to remit the case to the examiner to attend to any outstanding matters before the case could be sent for grant. I confirmed that I would grant a discretionary extension which would set the formal compliance deadline as 8 June.

The application and its scientific context

8 The application concerns agents which can be used to target a protein called VHZ. The VHZ genes encode phosphatases which have approximately 28% homology with the "phosphatase of regenerating liver" (PRL), a subgroup of protein tyrosine phosphatases (PTP). Phosphatases remove the phosphate moieties from tyrosine residues in proteins. The application indicates that it was known before the priority date in 2004 that VHZ is ubiquitously expressed within human tissues and located in both the cytosol and the nucleoli.

9 Healthy eukaryotic cells go through several stages of mitosis to generate two new daughter cells. During this cycle two checkpoints occur. These are termed G1/S and G2-M. G1 is known as a 'restriction point' where a cell "decides" whether it will remain in the resting state (G0) or prepare for division. If it moves through this checkpoint the cell is committed to division and enters the S phase (synthesis) when DNA replication occurs. Following the S phase the cell passes into the G2 phase where it continues to grow and prepares for cell division, mitosis, to take place in the M phase. The G2/M is the second checkpoint where the cell checks that a number of factors are in place for division to take place.

10 These stages of the cell cycle have been well established for several decades. It was also well known before the priority date that phosphorylation is a central mechanism regulating the cell cycle. Kinases, for example tyrosine kinases, add phosphate groups to tyrosine residues while phosphatases remove these groups. Together protein kinases and phosphatases play a role in regulating phosphorylation and therefore the cell cycle. The kinases and phosphatases have been the subject of considerable attention in cancer biology, as cancer represents a deviation from the normal cell cycle.

11 The application is based on the premise that the VHZ proteins function at the first restriction point, G1/S. In the G1/S phase several proteins come into play. I will briefly describe these here as they become relevant to the question of support. They are: p21 (Cip1/Waf1), cyclin-dependant kinase-4 (cdk4), retinoblastoma gene (Rb) and E-cadherin. Some of these proteins will promote cell cycle progression and drive the cell through the G1/S phase while others may inhibit it. For example, it is known that the Rb protein, a "tumour suppressor" protein, prevents progression of the cell cycle through G1 to the S phase. Cdk4 is a member of the cyclin kinases which regulate G1/S transition. One mechanism by which cdk4 is thought to do this is by phosphorylation of the Rb protein; Rb is active when it is hypophosphorylated. Cdk4 therefore can inhibit the activity of the Rb protein and consequently may promote

transition through G1/S phrase. The p21(Cip1/Waf1) protein is a cyclin-dependent kinase inhibitor which has tumour suppression properties (for example by inhibiting cdk4). It has been shown that p21 modulates S phase progression and prevents cell proliferation.

The invention

12 The claims at issue were filed on 21 March 2013 and contain 14 claims. There are 4 independent claims. Claim 1 reads:

> "*An anti-VHZ agent for use in the treatment, prophylaxis or alleviation of invasive or metastatic cancer in which VHZ is overexpressed*"

13 Claim 1 is of the format which is now established[1] as seeking protection for "second medical use" - that is where a claim to a medicine is characterised by its use to treat a particular disease or set of diseases.

14 The other independent claims, 9, 13 and 14, relate to methods of detecting metastatic cancer. No objections were raised against these claims by the examiner.

The law

15 A number of provisions of the Act are relevant to this case, namely the provisions on second medical use (S.4(A)(4)), support (S.14(5)(c)), added matter (S.76(2)), and the application of the European Patent Convention (S.130(7)).

16 Section 4(A)(4) reads:

> "*In the case of an invention consisting of a substance or composition for a specific use in any such method, the fact that the substance or composition forms part of the state of the art shall not prevent the invention from being taken to be new if that specific use does not form part of the state of the art*".

This provision was implemented in the Patents Act 2004 on 13 December 2007. Essentially, it means that if something was already known to be used as a medicine it can be claimed for use in the treatment of another different medical condition if that new use is novel and inventive. Such claims are conventionally termed "second medical use" claims. The same provision exists under the European Patent Convention (Article 54(5) EPC 2000). However, prior to the implementation of this provision it was possible to obtain protection for second medical use as a result of special formats of claims (Swiss claims) which were endorsed by both domestic and EPO case law. It is the view of the Intellectual Property Office that the implementation of section 4(A)(4) has not changed the scope of patent protection for second medical use claims. Rather, section 4(A)(4) now provides a statutory mechanism for the situation that existed prior to its implementation in primary patent legislation.

[1] Patent Practice Notice 3/10

17 Section 14(5)(c) reads:

> *The claim or claims shall:*
>
> *a....*
>
> *b...*
>
> *c be supported by the description; and*
>
> *d....*

18 Section 76(2) reads:

> *"No amendment of an application for a patent shall be allowed under section 15A(6), 18(3) or 19(1) if it results in the application disclosing matter extending beyond that disclosed in the application as filed"*

19 Section 130(7) of the Patents Act indicates the provisions of this Act *inter alia* in respect of support are the same as those of the European Patent Convention. It includes the phrase which reads:

> "*it is hereby declared that the following provisions of this Act, that is to say, sections 1(1) to (4), 2 to 6, 14(3), (5) and (6), 37(5), 54, 60, 69, 72(1) and (2), 74(4), 82, 83, 100 and 125, are so framed as to have, as nearly as practicable, the same effects in the United Kingdom as the corresponding provisions of the European Patent Convention*".

This means that, where appropriate, I should take account of decisions of the European Patent Office which the UK Courts and House of Lords have consistently indicated are persuasive.

20 A number of authorities were cited by the examiner. I also drew Mr Clegg's attention to the Court of Appeal's judgement in *Genentech Inc's patent* which I thought was relevant to the case in hand and is referenced in some of the authorities cited by the examiner. Mr Clegg indicated he was content for me to proceed on this basis. The authorities which I have considered are:

Regeneron Pharmaceuticals Inc & Bayer Pharma AG v Genentech Inc [2013] EWHC Civ 93 (Pat) (hereinafter referred to as "*Regeneron"*)

Medimmune Ltd v Novartis Pharmaceuticals UK Ltd, Medical Research Council [2011] EWHC 1669 (Pat) (*hereinafter referred to as "Medimmune")*

Conor Medsystems v Angiotech Pharmaceuticals [2008] UKHL 49 *(hereinafter referred to as Angiotech"*)

T609/02 Salk (EPO Boards of Appeal)

Prendergast's Applications [2000] RPC 446

Biogen Inc. v Medeva PLC [1997] RPC 1 (hereinafter referred to as "Biogen")

Schering Biotech Corp.'s Application [1993] RPC 249

Genentech Inc's patent [1989] RPC 147 (CA)

21 I note that the examiner cited the judgement of Floyd J in the High Court in *Regeneron* whereas Mr Clegg cited from the recent judgement of the Court of Appeal in that case. I am bound to follow the higher court which I note upheld the judgement of Floyd J.

Added matter

22 The examiner had objected that the phrase incorporated into the current version of claim 1 which reads "*...in which VHZ is overexpressed....*" represents added matter.

23 At the outset I should say that in many respects an added matter objection could be regarded as the converse objection to lack of support. If a feature introduced into a claim adds matter then it follows it was not supported by the description as filed. Nonetheless, there is a distinction between the two and lack of support might be considered a broader provision than added matter in respect of medical use claims. The examiner's concerns were two-fold. Firstly, he considered that the description does not demonstrate that VHZ overexpression exists in cancers other than breast cancer. Secondly, that the application does not unequivocally demonstrate that VHZ is overexpressed in MCF-7, the breast cancer cell line on which the majority of examples in the application are based.

24 The legal test for added matter is well established[2] . In effect, one has to look at what is disclosed, both explicitly and implicitly, in an amended application and determine whether this was clearly and unambiguously disclosed, explicitly or implicitly, in the application as originally filed.

25 In his submissions on this point Mr Clegg drew the distinction between the content of the application, its disclosure, and the requirement for experimental evidence. He said the test for added matter was concerned with disclosure, not experimental evidence. I would agree with that point.

26 Mr Clegg highlighted eight passages in the application[3] which he said provided adequate disclosure for the overexpression of VHZ in cancers other than breast cancer. For example, the passage on page 32 lines 16-25 which reads:

> "*Thus, detection of a high level of VHZ expression, amount or activity of VHZ in the cell may indicate that the cell is likely to be or become aggressive, metastatic or invasive. Similarly, if a cell has a low level of VHZ expression, amount or activity, the cell is not or is not likely to be aggressive, metastatic or*

---

[2] *Bonzel and Schneider (Europe) AG v Intervention Ltd* [1991] RPC 553

[3] (page 2 line 2, page 5 line 7, page 11 line 15, page 32 lines 16-20, page 33 lines 3-8, page 40 lines 5-10, and 27; page 46 lines 4-9, page 90 lines 7-9)

invasive. It will be appreciated that if the level of VHZ varies with the aggressiveness of a tumour, that detection of VHZ expression, amount or activity may also be used to predict a survival rate of an individual with cancer, i.e., high levels of VHZ indicating a lower survival rate or probability and low levels of VHZ indicating a higher survival rate or probability, both as compared to individuals or cognate populations with normal levels of VHZ. Detection of expression, amount or activity of VHZ may therefore be used as a method of prognosis of an individual with cancer."

27 A passage on Page 90, lines 5-7 reads "*Although the precise role that VHZ plays in tumor progression and cancer cell migration is not known, our data suggests that overexpression of VHZ or its elevated activity might be a crucial early event for local invasion*".

28 On reading the application it is clear that the major focus is breast cancer and I can therefore understand the examiner's concern about the reference to cancer *per se*. However, having carefully considered the application in its entirety I am led to conclude that it is not unreasonable to assume that VHZ overexpression is contemplated in cancers as a whole.

29 Having read the application as filed I am not struck by anything new when reading the amended version of claim 1. I am particularly minded of Mr Clegg's point about the distinction between disclosure and evidence concerning added matter which I regard as consistent with the case law. For this reason, I consider that the amendment of claim 1 to include the phrase "*in which VHZ is overexpressed"*, in relation to invasive or metastatic cancers, does not add matter.

Support

30 As I have mentioned, claim 1 is a so-called "second medical use" claim. This type of claim requires particular consideration in relation to lack of support. However, before looking at the law specifically on "second medical use", I think it is appropriate for me to consider three UK authorities, cited by the examiner, which together provide a strong framework for approaching the general issue of lack of support. They are *Genentech*, *Schering* and *Biogen* which incidentally all concerned biotechnology.

31 Genentech was the first biotechnology case to come before the Court of Appeal (CoA) in the relatively early days of the biotechnology era. The CoA noted that lack of support is not a ground which can be addressed after a patent is granted, unlike the similar provision of sufficiency, provided for by section 14(3) of the Act. As a consequence of this, the comments of Dillon LJ in *Genentech* have become a firm guiding principle for patent examiners, especially in new fields such as biotechnology. He said on page 236 line 50-page 237 line 3:

"*The Patent Office ought to have very clearly in mind that it is undesirable to allow claims the object of which is to cover a wide and unexplored field or where there is no disclosure in the specification which is in any way coterminous with the monopoly indicated in the claims*".

32 *Schering* specifically concerned lack of support. Here, Aldous J pointed out that the substance of a disclosure, rather than its form, was the key issue. He said at page 252 line 53-page 53 line 2:

> *"I do not believe that the mere mention in the specification of features appearing in the claim will necessarily be a sufficient support. The word "support" means more than that and requires the description to be the base which can fairly entitle the patentee to a monopoly of the width claimed."*

33 In *Biogen,* Lord Hoffmann made a substantive link between support and sufficiency, the latter being a point at issue in that case. His Lordship said at page 47 lines 45-48:

> "*But the substantive effect of section 14(5)(c), namely that the description should, together with the rest of the specification, constitute an enabling disclosure, is given effect by section 72(1)(c). There is accordingly no gap or illogicality in the scheme of the Act."*

34 Here, Lord Hoffmann's comments provide a legal basis for applying some of the principles established by the case law on sufficiency to the issue of lack of support. This is useful because sufficiency has been addressed in several authorities, notably *Regeneron* which was cited by the examiner and referred to extensively by Mr Clegg in the present case.

35 A fundamental point made in *Biogen* was that the scope of the claims should correspond to the technical contribution to the art that the application makes. In *Biogen*, Lord Hoffman also provided another important guiding principle that can be applied to questions of support by saying, at page 50 lines 42-45:

> "*It is not whether the claimed invention could deliver the goods but whether the claims cover other ways in which they might be delivered: ways which owe nothing to the teaching of the patent or any principle which it disclosed."*

36 I should comment on *Angiotech* as it was cited by the examiner. In *Angiotech* the issue before the House of Lords was obviousness, although the judgement does refer to sufficiency and support. I consider that my reasoning in this decision is consistent with the well established principles of sufficiency and support referred to by the House of Lords in *Angiotech.*

37 Next, I turn to the requirements of support for second medical use claims. A body of case law has firmly established the principle that for second medical use claims to be supported the application must provide adequate evidence of the effectiveness of the use of the substance in question as a medicine. This, in turn, boils down to the question of how much experimental evidence is required to provide support this type of claim. This is quite unusual in patent law because in the majority of technology areas experimental data is not usually a specific requirement for support. Section 4(A)(4) itself makes no reference to experimental evidence.

38 The crux of the issue therefore is what constitutes adequate evidence. In *Prendergast* second medical use claims were refused became the application contained no experimental data. In that case Neuberger J (as he then was) provided

some useful guidance for approaching the question of the level of experimental evidence required for support. He said on page 450 lines 12-14:

> "*the tests can, where appropriate, be very rudimentary. It would be wholly inappropriate, and indeed impractical, to lay down what the tests should be in each case, but it is clear that, in general, relatively rudimentary tests will do."*

39 It is clear from *Prendergast* and other case law (e.g.*Regeneron*) that clinical trial data is not essential to meet the requirements of support for second medical use claims. Supporting evidence can be in the form of *in-vivo, in-vitro* or *in-silico* data. However, the mere assertion that experiments had been carried out is unlikely to be sufficient.

40 In *Prendergast* and some of authorities cited in that case[4], the patent applications in question did not contain a shred of experimental data. This is not, however, the situation in the present application which clearly contains some experimental data. Rather, the issue in the present case is to what extent can evidence based on a set of experiments focussed on a particular disease, breast cancer, be applied more generally to providing a basis of support for the broader category of disease, namely cancer, in which the particular disease falls.

41 In essence, the law requires that I determine based on the information in the application and the views of the examiner and the applicant whether, on the balance of probabilities, the application provides sufficient evidence which supports the applicant's notion that VHZ plays a general role in cancer. Or to put it another way - whether the breath of the second medical use claims in question is commensurate with the teaching of the application in relation to VHZ and cancer, beyond breast cancer. In this regard the approach adopted by Kitchin LJ in the Court of Appeal in *Regeneron* is particularly helpful. In that case, Kitchin LJ indicates that the question to ask is whether the evidence is plausible or credible.

42 Before turning to the scope of the experimental evidence, I need to address two points in particular concerning the viability of the evidence before me. Firstly, there is the question of whether I should take account of the paper by Tang *et.al*[5] which is cited by the applicant in their correspondence and was also referred to by Mr Clegg in the hearing. This paper *was* published in 2010, after the priority date of the application. The case law*, for example Biogen and Prendergast*, makes it clear that when considering support the determinative date is the priority date. I therefore disregard any points made in relation to the Tang paper.

43 Secondly, I note that in Example 15 in the application the term "*data not shown*" is used. Example 15 is particularly relevant to the question of support and therefore I need to look at it carefully. It is not uncommon for the term "*data not shown*" to be used in scientific papers and therefore this term needs to be considered in context. In Example 15 (page 86 lines 19-21) the term is used in the following passage "*VHZ is found to be able to enhance cell proliferation rates*" *(data not shown)*. *To confirm this observation DNA synthesis rate is measured in these three cell lines...*".Thus, the example includes a description of experimental data which builds on the "*data*

---

[4] McManus's application [1994] FSR 558; Hoerrmann's application [1996] RPC 11; Consultant Supplier's Ltd's application [1996] RPC 11

[5] *Tang JP et.al. Mol Cancer 2010 9: 128*

not shown". On this basis, I have come to the conclusion that the reference to "*data not shown*" in Example 15 does not lessen the evidence provided by that example. It does not, to my mind, represent an unsubstantiated assertion which the case law on second medical use indicates cannot be regarded as relevant for establishing support.

44 I now turn to the examiner's objection that the claims in question are not supported. Essentially, the examiner argues that the application only provides evidence concerning breast cancer. Furthermore, he considers that the evidence in relation to breast cancer is only partial and does not prove that anti-VHZ agents would be effective against all breast cancers. This is summarised in a passage on page 2 of his prehearing report (28 March 2013) which reads:

> "*It is considered that there is no support in the application as filed that anti-VHZ agents could be used to treat anything other than invasive breast cancer. There is no evidence that all other metastatic and/or invasive cancers (which may or may not over-express VHZ) may be susceptible to such treatment. Given that the description at page 11 states that "...VHZ is predominantly associated with invasive human epithelial breast cancer cells..." and that "Over expression of VHZ protein is found in the centrosome or throughout the cytoplasm of human breast cancer samples...", there is no evidence that VHZ over-expression is even associated with other cancers much less that an anti-VHZ agent would be useful in their treatment*".

45 At this juncture I think it is important to bear in mind two points. Firstly, that claim 1 places a limiting condition that the cancer must be characterised by the overexpression of VHZ. Secondly, while claim 1 refers to "anti-VHZ agents" the critical issue for me to consider is whether the application contains support for the expression of this gene in cancers rather than to attach any significance to the agents which may target it. The description provides an ample level of information about how anti-VHZ agents could be made, reciting references to the general technologies which can be used to inhibit gene products, e.g. RNA interference and antibody technology. From this, I think it is safe to assume that agents against a VHZ expression product (e.g. RNA or protein), which may subsequently be used therapeutically, could be produced by conventional techniques.

46 Mr Clegg's basic legal point was that if an application discloses a beneficial property of a general principle or a class, then the claims should be entitled to cover that general principle or class. He highlighted the principle of "plausible or credible" referred to in R*egeneron.* The kernel of Mr Clegg's submission in relation to the application was that:

> "*the experiments should not be read in the context of breast cancer, they are about VHZ overexpression and what that teaches you*".

47 He pointed again to the passage in the description on page 90, lines 5-7 which reads "*our data suggests that overexpression of VHZ or its elevated activity might be a crucial early event for local invasion*".

48 Mr Clegg submitted that the application provided evidence of the common beneficial property of the class of anti-VHZ agents encompassed by claim 1. He referred me to

the points he made previously in relation to added matter with which I agree – that there is sufficient disclosure in the application about cancer.

49 In expanding his arguments Mr Clegg drew my attention to a number of passages in *Regeneron*, for example the passages in paragraphs 98-100 which read:

> [98] *"It is permissible to define an invention using general terms provided the patent discloses a principle of general application in the sense that it can reasonably be expected the invention will work with anything falling within the scope of these terms."*
>
> *[100] "It must therefore be possible to make a reasonable prediction the invention will work with substantially everything falling within the scope of the claim or, put another way, the assertion that the invention will work across the scope of the claim must be plausible or credible. The products and methods within the claim are then tied together by a unifying characteristic or a common principle. If it is possible to make such a prediction then it cannot be said the claim is insufficient simply because the patentee has not demonstrated the invention works in every case*".

50 Mr Clegg also referred to the decision of the EPO Boards of Appeal in *Salk* which was referred to by Kitchin LJ in *Regeneron*. The relevant passage in *Salk* reads:

> [9]"....*It is required that the patent provides some information in the form of, for example, experimental tests, to the avail that the claimed compound has a direct effect on a metabolic mechanism specifically involved in the disease, this mechanism being either known from the prior art or demonstrated in the patent per se. Showing a pharmaceutical effect in vitro may be sufficient if for the skilled person this observed effect directly and unambiguously reflects such a therapeutic application (T 241/95, OJ EPO 2001, 103, point 4.1.2 of the reasons, see also T 158/96 of 28 October 1998, point 3.5.2 of the reasons) or, as decision T 158/96 also put it, if there is a "clear and accepted established relationship" between the shown physiological activities and the disease (loc. cit.)*".

51 I regard the judgement in *Regeneron,* which *inter alia* concerned the issue of insufficiency, as particularly relevant to the present case. *Regeneron* concerned the question of evidence relating to particular set of diseases, cancer, to a more general class of which cancer displayed some characteristics, diseases characterised by angiogenesis. Moreover, I consider that the comments of the EPO Boards of Appeal in *Salk*, endorsed by the CoA in *Regeneron*, regarding the relevance of information about metabolic mechanisms are particularly applicable to the central issue in the present case. A central issue in the present case is whether evidence, although obtained from experiments on a limited range of cell types, can nonetheless be used to support a general concept that applies to a broader range of cell types if the experiments provide information about a mechanism which underlies the general concept.

52 The experiments in the application involved investigating VHZ expression in a breast cancer line (MCF-7), a non-cancerous breast epithelial cell line (MCF-10A), a normal

rat kidney (NRK) cell line and an epithelial carcinoma cell line (A431) (apparently derived from the epidermis).

53 The critical question is then whether these experiments provide sufficient evidence for a role of VHZ in cancer *per se*. The issue is finely balanced but on the facts of the case I think they do. It is my view therefore that the application provides the requisite support for claim 1. My reasons for coming to this conclusion are as follows.

54 Firstly, as I have mentioned in relation to the issue of added matter, in my view it is evident from the disclosure of the application that, in substance, the treatment of cancer *per se* is contemplated (I consider that the header "Breast Cancer" on page 46 does not necessarily limit the meaning of 'cancer' in the paragraphs which immediately follow it).

55 Secondly, Mr Clegg emphasised that the experiments included work on not only MCF-7 but also on NRK cells. I am minded that information which leads to an understanding of normal growth can naturally inform the understanding of processes involved in aberrant growth, namely cancer. I consider that, taken together, the data arising from work involving NRK cells and the non-cancerous breast cancer line MCF-10A, as well as experiments involving A431cells, can contribute to the evidence about the role of VHZ in cancer.

56 Thirdly, the application details a range of experiments which show the relationship of VHZ with several of the proteins that are associated with the G1/S phase. Example 15, (page 86) notably using both the breast cancer line MCF-7 and NRK cells, indicates that VHZ can enhance cell proliferation. Example 16 is more specific and says on page 86 line 29-page 87 line 7:

> "*we found that VHZ could down regulate the tumour suppressor gene p21 Waf1/Cip1 and upregulate cyclin-dependant kinase (cdk) 4"....Consistent with this we showed that overexpression of VHZ phosphatase could indirectly lead to an accumulation of phosphorylation of Rb at residues Ser780, Ser795 and Ser807/811 as assessed by phospho-specific antibodies..*"

57 Fourthly, Mr Clegg drew my particular attention to Example 18 (page 88) and said that it provides evidence that VHZ overexpression is associated with a loss of E-cahderin which is known to be associated with epithelial-mesenchymal transition (EMT). In turn, EMT is characteristic of oncogenesis. I have no good reasons to doubt Mr Clegg's assertions based on this data.

58 Mr Clegg submitted that the data is "on the point" of the metabolic mechanism, i.e. it proves a metabolic mechanism and explains *why* a VHZ agent would work. He submitted that this reasoning was in line with *Salk* and *Regeneron*. I think there is force in this point if one looks at the experiments against the background of what was already known in the field.

59 It is clear that the cell cycle had been very well characterised for many years before the priority date of the application. The application describes the interplay of proteins which function at the particular part of the cell cycle in question, the G1/S phase. Although the application does not go into much detail about these proteins, it is also clear that the functions of many of them, e.g. cyclin dependant kinases, tyrosine

phosphatases and the retinoblastoma (Rb) protein, had been well described. In my view Examples 15-18, in particular, provide a logical basis from which reasonable assumptions about the impact of VHZ on the proteins that regulate G1/S can be made. To my mind therefore it follows that the application teaches something about the relationship of VHZ and the cell cycle in general.

60 I should point out at this juncture that I consider an important distinction exists between the evidence of the mechanism for VHZ in cancer and evidence of the impact that anti-VHZ agents may have on cancer cells in general. If the application had only provided evidence of the effects of anti-VHZ agents on the cell surface of breast cancer cells then I would agree with the examiner that the application would only provide support for treating breast cancer. For example, if the evidence in the application had been limited to the investigation of anti-VHZ agents in inhibition assays or in expression studies on breast cancer cells, such as the immunohistochemistry experiments in Example 9 (page 84), without evidence of the intracellular role of VHZ, then it would not be reasonable to draw general conclusions about the potential impact of VHZ agents in cell growth. But to my mind, the application provides more. As I have said, I consider it provides evidence of the role of VHZ in the general mechanisms of cell growth. On this basis I consider that reasonable assumptions can be made about the role VHZ may play in aberrant cell growth, namely cancer.

61 As a “check” I asked Mr Clegg how he would explain his point to the lay person who may be inclined to think of cancers as very different chaotic systems and therefore might wonder how therapies for one type of cancer, breast cancer, could be applied to another, for example brain or bowel cancers. He responded by saying it is a question of markers of cancer. He reiterated his central submission from which I understood his point to be that the key issue is the fact that VHZ overexpression becomes a marker of a cancer and it is cancers characterised by this overexpression of VHZ that an anti-VHZ agent would be effective against. He drew a comparison from the well known cancer drug Herceptin which is used to treat certain types of cancer which are characterised by the marker that Herceptin targets. While I suspect that the mechanism of Herceptin action is better characterised than the role of VHZ at issue in this case, I nonetheless take Mr Clegg’s point about markers of cancer. As I have mentioned above, the independent claims are restricted to cancers in which VHZ is overexpressed. In one sense, the issue is circular - that if cancers exist which are not characterised by VHZ overexpression then agents against VHZ are unlikely to have a practical use in treating cancer which do not overexpress VHZ. On the other hand, if VHZ is overexpressed in cancers then, on the basis of the evidence in the application, it would seem plausible that inhibiting VHZ would impair cancerous cell growth.

62 Minded of the recent guidance of the Court of Appeal in *Regeneron*, I consider on the basis of information before me it is credible that at the priority date the skilled addressee could have expected from reading the application that anti-VHZ agents could be used to treat not only breast cancer but other cancers. I am also of the opinion that it is reasonable to assume that if in future therapies on cancers involving VHZ agents should prove successful then they would owe something to teachings of the application in suit. I therefore consider that my finding is consistent with Lord Hoffmann’s guidance in *Biogen* to which I have previously referred. The applicant

has, to my mind, adequately demonstrated the role of a particular protein, VHZ, at a particular point in the cell cycle, the G1/S restriction point, and the claims reflect that. Therefore, I do not believe that the applicant is unduly monopolising an unexplored field in the way which concerned Dillon LJ in *Genentech*.

63 I think the comments of Kitchin LJ in *Regeneron* neatly summarise the point which is fundamental to considering the issue of support for a patent claim. He said at paragraph 96:

> "*...it is now well established that the scope of the monopoly, as defined in the claims, must correspond to the technical contribution the patentee has made to the art*".

64 I believe that the breadth of the claims in the present application reasonably reflect the contribution the application makes to the art in relation to the involvement of VHZ in cancer.

Decision

65 I hold that claim 1, as amended, does not include added subject matter. I also hold that claim 1 and claims 2-8 are supported.

66 I therefore remit the case to the examiner for further processing as it appears some consequential amendments to the description may be necessary. I am aware that the first discretionary compliance period under Rule 108 (3) expires on 8 June and I would envisage that matters can be completed before that date. If for some good reason this is not possible then, in principle, I would allow a further discretionary extension under Rule 108(3).

Appeal

67 Any appeal must be lodged within 28 days.

J HOULIHAN
Deputy Director acting for the Comptroller