THE SUPREME COURT OF APPEAL OF SOUTH AFRICA

JUDGMENT

REPORTABLE
Case No: 468/2013

In the matter between:

PHARMA DYNAMICS (PROPRIETARY) LIMITED **APPELLANT**

and

BAYER PHARMA AG (FORMERLY BAYER SCHERING PHARMA AG) **FIRST RESPONDENT**

BAYER (PROPRIETARY) LIMITED **SECOND RESPONDENT**

Neutral citation:	*Pharma Dynamics (Pty) Ltd v Bayer Pharma AG* (468/13) [2014] ZASCA 123 (19 September 2014).
Coram:	Brand, Cachalia, Wallis, Mbha JJA *et* Mathopo AJA
Heard:	**28 August 2014**
Delivered:	**19 September 2014**

Summary: Patents Act 57 of 1978 – whether appellant's product constitutes infringement of respondents' patent – counterclaim for revocation of patent – whether invention for which protection claimed in the patent involves an inventive step required by s 25(1) of the Act – whether patent qualifies as a true 'divisional patent' in terms of s 37 of the Act.

ORDER

On appeal from: The Court of the Commissioner of Patents of South Africa (Pretorius J, sitting as Commissioner of Patents):
The appeal is dismissed with costs, including the costs of two counsel.

JUDGMENT

Brand JA (Cachalia, Wallis, Mbha JJA *et* Mathopo AJA concurring):

[1] This is an appeal against the judgment and order of Pretorius J sitting as the Commissioner of Patents. The first respondent, Bayer Pharma Aktiengesellschaft, formerly known as Schering AG, is the patentee of South African Patent No 2004/4083 for an invention entitled 'Pharmaceutical combination of ethinylestradiol [EE] and drospirenone [DSP] for use as a contraceptive' (the 2004 patent). The second respondent, Bayer (Pty) Ltd, has been licenced to use the invention in South Africa. They will jointly be referred to as 'Bayer'. The appellant, Pharma Dynamics (Pty) Ltd (Pharma) is a local distributor of generic pharmaceuticals.

[2] As predicted by the concise description in its title, the 2004 patent concerns a female combination oral contraceptive containing the active pharmaceutical ingredients, DSP and EE. It was filed in 2004 in terms of s 37 of the Patents Act 57 of 1978 (the Act) as a so-called 'divisional patent', based on patent 2002/1668, as its 'parent patent'. By virtue of the provisions of s 37, the priority date of the 2004 patent was ante-dated to 31 August 1999, which is the priority date of its 2002 parent patent.

[3] In March 2011, Pharma obtained approval from the Medical Control Council to import and sell an oral contraceptive called Ruby. This product is the generic equivalent of the Yasmin product sold by Bayer under the 2004 patent. Alleging that

the sale of Ruby constituted an infringement of claim 1 of the 2004 patent, Bayer approached the court a quo for an interdict and ancillary relief. Pharma denied that Ruby infringed the patent. It also denied that the 2004 patent was valid and counterclaimed for its revocation. The court a quo held, however, that the 2004 patent was valid and that Ruby infringed it. In consequence it granted the relief claimed by Bayer and dismissed Pharma's counterclaim, in both instances, with costs of suit. The present appeal against that order is with the leave of the court a quo.

[4] The case for Pharma on appeal is that, properly interpreted, claim 1 of the patent in suit – which is the only claim relevant – does not include within its scope the allegedly infringing Ruby product. For its attack on the validity of the patent, Pharma relied firstly on the ground that the invention claimed in the specification of the patent lacks an inventive step, or, in patent parlance, it relied on the basis of obviousness. Secondly, Pharma contended that, in any event, the 2004 patent is invalid on the ground that it is not a true 'divisional' of the 2002 parent patent. In consequence, so Pharma's contention went, the 2002 patent lacked novelty in the light of the disclosures in the 2002 patent. Since all these contentions are largely dependent on an interpretation of the specification and especially claim 1 of the 2004 patent, I find it appropriate to reflect on the broad principles of patent interpretation as established by authority.

Foreign judgments

[5] However, before doing so, there is the matter of foreign judgments, which attracted a fair deal of debate during argument before us. It appears that the patent in suit had been the subject of litigation in various jurisdictions. Unsurprisingly Bayer referred us to judgments in the United Kingdom by the high court in *Gedeon Richter plc v Bayer Schering Pharma AG* [2011] EWHC 583 (Pat) and the Court of Appeal in *Gedeon Richter plc v Bayer Pharma AG* [2012] EWCA Civ 235 and in Australia by the Federal Court of Australia General Division in *Generic Health (Pty) Ltd v Bayer Pharma AG* [2014] FCAFC 73 where the patent in suit survived an attack based on

the premise that it lacked an inventive step. Pharma, on the other hand, referred us to the judgment of the Technical Board of Appeal of the European Patent Office in *Bayer Pharma AG v Teva Pharmaceutical Industries Ltd* (Case No 0598/12) where the application for the revocation of the patent was upheld. But as I see it, we must decide the matter on the evidence before us. Helpful as these foreign cases may be on matters of law, we can derive no guidance from them on issues of fact.

Approach to Interpretation

[6] This brings me back to the principles of interpretation. To begin with, there is the tenet of patent construction which is encapsulated in the oft quoted statement by Trollip JA in *Gentiruco AG v Firestone SA (Pty) Ltd* 1972 (1) SA 589 (A) at 614B-H that:

'. . . [T]he rule of interpretation is to ascertain, not what the inventor or patentee may have had in mind, but what the language used in the specification means, ie, what his intention was as conveyed by the specification, properly construed . . . since he is presumed to have intended what his language means. To ascertain that meaning the words used must be read grammatically and in their ordinary sense . . . The specification like any other document must be read as a whole.'

(See also *Cipla Medpro (Pty) Ltd v Aventis Pharma SA and Related Appeal* 2013 (4) SA 579 (SCA) para 14.)

[7] Yet, established authority also reveals that the reference to 'the ordinary meaning of words' must not be understood as an exercise in focusing on each word in isolation, but by viewing them in the context of the patent as a whole (see eg *Aktiebolaget Hässle & another v Triomed (Pty) Ltd* 2003 (1) SA 155 (SCA) para 8). Essentially the same principle was expressed with admirable clarity in the following statement by Lord Diplock in *Catnic Components Ltd & another v Hill & Smith Ltd* [1982] RPC 182 (HL) at 242 – referred to with approval in the many judgments of this court cited in *Aktiebolaget Hässle (*para 8):

'. . . A patent specification should be given a purposive construction rather than a purely literal one derived from applying to it the kind of meticulous verbal analysis in which lawyers are too often tempted by their training to indulge. The question in each case is: whether

persons with practical knowledge and experience of the kind of work in which the invention was intended to be used, would understand that strict compliance with a particular descriptive word or phrase appearing in a claim was intended by the patentee to be an essential requirement of the invention so that *any* variant would fall outside the monopoly claimed, even though it could have no material effect upon the way the invention worked.'

[8] Or, in the words of Corbett JA in *Multotec Manufacturing (Pty) Ltd v Screenex Wire Weaving Manufacturers (Pty) Ltd* 1983 (1) SA 709 (A) at 721C-E:

'. . . The Court should always guard against too "textual" an approach in the interpretation of claims in a patent specification. It is true that it is in the claims that a patentee stakes out and defines his monopoly; and that the claims must be looked at in order to determine whether an infringement has taken place. But by peering too closely at the language of a claim the Court may overlook an infringement which takes the substance of the invention.'

[9] Finally, with regard to interpretation, I start out from the well-established premise, that a patent specification is a statement by the patentee, addressed to those 'skilled in the art', in which he informs them of what he or she claims to be the essential features of the invention for which a monopoly is claimed. Consequently, a patent specification must be construed with reference to the state of knowledge of those skilled in the art at the time of the priority date of the patent in issue. Accordingly, in order to enable the court to construe the specification properly, it must be instructed by expert witnesses as to the state of the art in the field of the invention in order to place the court as near as may be possible to the position of those skilled members of the public to whom it is addressed, as at the relevant date (see eg *Sappi Fine Papers (Pty) Ltd v ICI Canada Inc (Formerly CIL INC)* 1992 (3) SA 306 (A) at 318I-319E).

Background

[10] For that purpose, two experts in the field were called to give evidence at the trial, namely, Prof Martyn Davies on behalf of Bayer and Dr Peter Rue on behalf of Pharma. They were largely in agreement that the addressees of the patent would be a broad interdisciplinary product formulation team of a pharmaceutical company, led

by an experienced scientist and including biological pharmacologists, toxicologists, clinicians and so forth. For the sake of brevity, these addressees of the patent in suit were referred to at the trial and in argument as ‘the skilled formulator’. I propose to follow that example. Broadly speaking, the two experts were also in agreement as to the state of the knowledge of that skilled formulator as at the priority date, ie 31 August 1999. In this way the following background had been established.

[11] An active pharmaceutical ingredient (API) administered to humans orally, passes down the gastro-intestinal tract and is absorbed into the bloodstream. For present purposes we can concentrate on two parts of that tract, to wit, the stomach and the small intestine. The stomach is highly acidic with a generally accepted pH range of between 1 and 3. The stomach lining is not designed for absorption. The primary purpose of the stomach is after all not to absorb, but to digest the ingested food. By contrast, the small intestine is less acidic – generally accepted as ranging from pH 5 to 7 – and primarily designed for absorption into the bloodstream. The API can only be absorbed into the bloodstream once it is in solution, ie once it has been dissolved. The quantity of API absorbed into the bloodstream and eventually becoming available at the point of the human body where it is required for treatment of the individual, is said to be bioavailable. Bioavailability therefore describes the quantity of the drug, expressed as a percentage of the dose administered, that becomes available for treatment.

[12] Because of the arrangement of the gastro-intestinal tract, the API must pass through the highly acidic conditions in the stomach before it reaches the small intestine where it can be absorbed, ie before it becomes bioavailable. It stands to reason that the longer the API remains in the stomach, the more it will be affected by those conditions. The skilled formulator would have been aware that the residence time of the API in the stomach might vary substantially. With regard to a particular individual it would be influenced by a number of factors, including whether the individual had eaten or fasted, the nature of the diet and so forth. Moreover, apart from this intra-individual variability, there would be inter-individual variability in

residence time. All in all stomach residence may vary between 30 minutes and 4,5 hours with a meantime of 90 minutes. If the API is therefore immediately released once it reaches the stomach, it may spend anything between 30 minutes and 4,5 hours in that highly acidic condition.

[13] A formulator charged with a formulation for an API will invariably conduct formulation tests in the laboratory, referred to as in vitro tests. These are, inter alia, aimed at establishing, among other things, the solubility of the drug and its stability under acidic conditions. The rate of dissolution may be studied in vitro using standard dissolution tests. Such tests are routinely used in the pharmaceutical industry. The 'USP XXIII Paddle Method' referred to in claim 1 of the 2004 patent – to which I shall presently return – is one of these standard methods of testing the rate of dissolution, which any skilled formulator would understand.

[14] As drugs administered orally need to dissolve in the gastro-intestinal tract in order to be effective, drug candidates that exhibit poor solubility in vitro will be considered a risk for development as they may show poor bioavailability in vivo, ie in the human body. The dissolution rate of a drug can, however, be increased. So, for example, the particle size of the drug can be reduced – known as micronisation – or the drug can be dissolved and sprayed onto the surface of inert carrier particles. Since these two methods of improving the rate of dissolution are expressly referred to in the 2004 patent, I shall return to them in later discussion.

[15] If an API is unstable in acidic conditions, ie if it is acid labile, a significant portion of the drug may be degraded or isomerised in the stomach, which would in turn reduce its bioavailability. This would of course be a contraindication for increasing the dissolution rate of an API known to be acid labile. The reason for the 'of course' is that the sooner the drug dissolves in the acidic conditions of the stomach, the more severe the influence of those conditions will probably be. Moreover, given the potential of both intra and inter individual variability in stomach

residence time, the formulator would have to produce a formulation that could cope with the longest possible exposure to the acidic environment of the stomach.

[16] One way of overcoming the problem of isomerisation in the stomach is to increase the dosage of API administered. That, however, could result in an overdose. The skilled formulator would have known that, especially with reference to a drug which is used regularly, as in the case of a contraceptive, overdose could be particularly detrimental to the user. Another way of resolving the problem of acid lability is to protect it from the acidic environment in the stomach by means of an enteric coating. Enteric coatings act as an impermeable barrier around the API and prevent the acid content of the stomach from coming into contact with the underlying API. As at the priority date, the skilled operator would have known that there were a number of different enteric coatings available for this purpose.

[17] Also well-known, since at least the 1960s, was the fact that DSP in combination with EE could be used as a contraceptive. In vitro tests had shown, however, that DSP has the two features that presented a particular challenge to formulators, namely that it was both poorly soluble and acid labile. Moreover, because it was destined for use as a contraceptive, excessive dosage was a potential problem, which indicated small dosages. To add to the formulator's difficulty, a contraceptive has to be formulated so that it is a 100 per cent effective at inhibiting ovulation, given that the consequence of an ineffective dose could be an unwanted pregnancy. This added demand does not present itself, for instance, with analgesics and antibiotics. With DSP it was therefore necessary to establish a dosage which achieved this high degree of reliability. What the formulator would have known in sum was that in all these circumstances, it was of cardinal importance to ensure, not only that each tablet contained the right dosage at the point of administration, but also that as little as possible of the dosage was not lost on its way to the site of absorption in the small intestine.

[18] The two experts who testified at the trial were generally in agreement that the results of in vitro tests in themselves would have indicated a development of a small dosage of DSP with increased solubility – also described as rapid dissolution – eg by way of micronisation, but protected from the acid in the stomach by an enteric coating. The record of the in vitro tests carried out by Bayer in fact showed this. From here on, the two experts, however, parted company. Dr Rue's view was that the skilled formulator would not have decided to protect DSP with an enteric coating unless and until the results of the in vitro experiments had been confirmed by in vivo tests on humans. Even with drugs known to be highly acid labile, so he said, in vivo tests are routinely conducted. The reason, he said, was the known fact that one cannot accurately predict the in vivo bioavailability of the drug purely from in vitro experiments. Accordingly, he concluded that despite the results of the in vitro tests, the skilled formulator would routinely have performed an in vivo test with both enteric coated and uncoated DSP at an early stage of the development process. In vivo tests would then have shown, as we now know with the experience of hindsight, that good bioavailability could be attained with DSP unprotected by an enteric coating. Prof Davies, on the other hand, was of the view that in the light of the in vitro results, the skilled formulator would have regarded in vivo tests with uncoated DSP as wasteful of both time and money. This is particularly so, because in vivo tests, he said, are costly and time consuming. A skilled formulator would therefore not embark on this road with no expectation of success which was what the in vitro experiments predicted.

[19] How Bayer actually came to realise that DSP need not be protected by an enteric coating, emerges from the 'inventors' story' that derived from the documents referred to by both experts during their evidence at the trial. In broad terms the story went as follows. During April 1983, Dr Johannes Tack, who later became the Head of Pharmaceutical Development at Bayer – but at that time, still a junior researcher – was charged with the task of developing an oral tablet formulation of one milligram DSP. Results of in vitro tests steered him in the direction of an enteric coating. For the next four years scientists at Bayer thus conducted pre-formulation experiments

with enteric coated DSP exclusively. Results achieved by in vivo studies during this period, both with dogs and humans, were encouraging to the formulation team. Of some concern to them, however, was the inter-subject variation in these results. To address the possibility that these variances could be caused by the enteric coating that they used, they decided to do what was referred to in evidence as a three arm bioavailability test, which was done during the first term of 1988.

[20] Broadly speaking, the three arm test compared the bioavailability of DSP when administered in three forms: (a) intravenously – where absorption plays no role; (b) through enteric coated tablets; and (c) through tablets which were not enteric coated at all, and the DSP is thus immediately released in the stomach. Based on the results of in vitro studies, the formulation team clearly had no anticipation of success for the uncoated formulation. However, the surprise came when the bioavailability of the uncoated formulation proved to be statistically no different from that of the enteric coated drug.

[21] What must also be borne in mind at this juncture is that, although enteric coatings perform the positive function of protection against acid in the stomach, they had known disadvantages. First of these is that it delays absorption until it is finally dissolved in the small intestine. Hence it also delays the onset of action of the drug. The second and related problem is that the period of delay would be the subject of inter and intra-patient variability which is coupled to the residence time of the protected drug in the stomach. This again is of particular significance with a drug intended for contraception where it is undesirable to leave large gaps in the sequence of administration. In the light of these known disadvantages of an enteric coating and consequent delayed release of the drug, skilled formulators of Bayer realised the benefits of an immediate release of DSP. In consequence, the formulation team at Bayer subsequently redirected its research and development from coated to uncoated DSP, which is the form in which its Yasmin product was eventually marketed.

[22] In this light Prof Davies contended that the invention covered by the patent is the following (p 2 137):

'The very fact that against all expectations for a drug which is poorly soluble such as drospirenone and which is acid labile, against all expectations that if you used a rapid dissolution, a formulation that achieves a rapid dissolution, as per claim 1 of the 2004 specification . . . what you get is good bioavailability, in other words, good absorption in vivo. That is against all expectation due to the acid lability of the drug. So that is the inventive step.'

And at 2 504:

'There was a research proposal which they [the formulating team at Bayer] undertook, there was no expectation of success and they found to their surprise that they had a formulation which was rapidly dissolving on a poorly soluble acid labile compound good bioavailability in vivo against all experience, against all of the scientific knowledge that they had and we still cannot understand how it works. . . .'

[23] Dr Rue disagreed. In his view the fact that a rapidly dissolving micronised form of DSP, known to be acid labile, would not in fact degrade in vivo would have been experimentally determined by the skilled formulator through in vivo tests performed as a matter of routine at an early stage of the development. The three arm test eventually conducted by Bayer, so he testified, should have been done as a matter of routine at an earlier stage. Had this been done, the 'problem' contemplated by Bayer in the light of the in vitro results, would routinely have been established to be no real problem at all. His answer to Prof Davies' view that the invention, protected by the patent in suit served to resolve a particular problem was therefore in short that the skilled formulator would have known at an early stage that the perceived problem was not a real problem at all.

Infringement

[24] Against this background I can now turn to the question: does Pharma's Ruby product constitute an infringement of claim 1 of the 2004 patent? In *Letraset Ltd v Helios Ltd* 1972 (3) SA 245 (A) at 274G-H, the approach to this question was formulated as follows:

‘The determination of the question as to whether or not plaintiff has proved an infringement of his patent turns upon a comparison between the article . . . involved in the alleged infringement and the words of the claims in the patent. If the article or process falls within the ambit of the claims, properly construed; an infringement is proved. But the article or process will not be regarded as falling outside the scope of the claims if such differences as the comparison may disclose are not matters of any substance. In making the comparison the law looks at the essence of what is contained in the claim and will not allow what is described as the “pith and marrow” of the protected invention to be pirated. The evaluation of what is the substance or essence of an invention is a matter for the “good sense” of the judicial tribunal seized with the enquiry.’

[25] Claim 1 of the 2004 patent is formulated as follows:

‘A pharmaceutical composition comprising:

as a first active agent drospirenone in an amount corresponding to a daily dosage, on administration of the composition, of from about 2 mg to 4 mg, and

as a second active agent ethinylestradiol in an amount corresponding to a daily dosage of from about 0.01mg to 0.05 mg,

together with one or more pharmaceutically acceptable carriers or excipients,

wherein at least 70% of said drospirenone is dissolved from said composition within 30 minutes, as determined by USP XXIII Paddle Method II using water at 37ºC as the dissolution media and 50 rpm as the stirring rate.’

[26] It is common cause between the parties that this claim can be divided up into the following five features or integers:

A A pharmaceutical composition comprising:

B as a first active agent drospirenone in an amount corresponding to a daily dosage, on administration of the composition, of from about 2 mg to 4 mg;

C as a second active agent ethinylestradiol in an amount corresponding to a daily dosage of from about 0.01mg to 0.05 mg;

D together with one or more pharmaceutically acceptable carriers or excipients; and

E wherein at least 70% of said drospirenone is dissolved from said composition within 30 minutes, as determined by USP XXIII Paddle Method II using water at 37ºC as the dissolution media and 50 rpm as the stirring rate.

[27] It was not in dispute that Pharma's product includes integers A-D of the claim. The debate therefore turned on integer E. In broad outline the debate went along the following lines: according to the interpretation contended for by Bayer, the claim includes within its scope, DSP having the rapid dissolution rate specified in accordance with a known method of determination without an enteric coat, no matter how that dissolution rate had been achieved. By contrast, the interpretation relied upon by Pharma is that the claim is limited to the achievement of the specified rapid dissolution by way of micronisation on DSP (or of the possible alternative method of dissolving DSP in a suitable solvent and spraying the solution onto the surface of an inert carrier).

[28] In this regard it is common cause that the DSP used in the manufacture of Pharma's Ruby product attains the dissolution rate specified in integer E, but that it is not provided in micronised form or dissolved in a solvent and then sprayed onto the surface of inert carrier particles. Instead a solution containing the DSP is added as a bulk liquid which is distributed uniformly throughout the granules used in the formulation by means of a high speed mixer or granulator. Hence it is clear that if the interpretation contended for by Bayer is accepted, Ruby falls within the compass of integer E and hence of the claim – but not if Pharma's interpretation of the claim is sustained.

[29] Bayer's case is that claim 1 protects the invention described by Prof Davies. The contrary position taken by Dr Rue and Pharma is that if there was indeed an invention as described by Prof Davies - which they denied – that is not the invention covered by claim 1. Although directly contradictory, each party found support for its interpretation in the body of the patent specification, which reads in relevant part, under the heading 'Detailed disclosure of the invention':

‘Drospirenone . . . is a sparingly soluble substance in water and aqueous buffers at various pH values. Furthermore, drospirenone is rearranged to an inactive isomer under acid conditions and hydrolysed under alkaline conditions. To ensure good bioavailability of the compound, it is therefore advantageously provided in a form that promotes rapid dissolution thereof.

It has surprisingly been found that when drospirenone is provided in micronized form . . . rapid dissolution of the active compound from the composition occurs in vitro (“rapid dissolution” is defined as the dissolution of at least 70% over about 30 minutes . . . of drospirenone from a tablet preparation containing 3 mg of drospirenone in 900 ml of water at 37ºC determined by the USP XXIII Paddle Method using a USP dissolution test apparatus 2 at 50 rpm). Instead of providing the drospirenone in micronized form, it is possible to dissolve it in a suitable solvent, e.g. methanol or ethyl acetate, and spray it onto the surface of inert carrier particles followed by incorporation of the particles containing drospirenone on their surface in the composition.

Without wishing to be limited to any particular theory, it appears that the in vitro dissolution rate of drospirenone is connected to the dissolution rate in vivo resulting in rapid absorption of drospirenone in vivo on oral administration of the compound. This is an advantage because isomerization of the compound in the gastric environment and/or hydrolysis in the intestine is substantially reduced, leading to a high bioavailability of the compound. . . .

The composition of the invention may be formulated in any manner known in the pharmaceutical art. In particular, as indicated above, the composition may be formulated by a method comprising providing drospirenone and, if desired, ethinylestradiol in micronized form in said unit dosage form, or sprayed from a solution onto particles of an inert carrier in admixture with one or more pharmaceutically acceptable excipients that promote dissolution of the drospirenone and ethinylestradiol so as to promote rapid dissolution . . . on oral administration.’

[30] On Pharma’s construction of these paragraphs the ‘surprising finds’ made were, that when DSP is provided in micronised form (or dissolved and sprayed onto the surface of the particles of an inert carrier), rapid dissolution of the active compound from the composition in vitro is achieved. With regard to the contrary interpretation contended for by Bayer – ie that it covers the invention described by Prof Davies – Pharma pointed out that there is no indication that the ‘surprising finds’

relate to rapidly dissolving DSP leading to good bioavailability in vivo without the need for it to be protected by an enteric coating. In fact, so Pharma argued, the specification does not even refer to the subject of enteric coatings at all. Its only topic of discussion is the rapid dissolution of DSP and the two methods in which this can be attained.

[31] I do not believe, however, that this is how the skilled addressee would understand the specifications. First of all, the fact that rapid dissolution could be achieved in vitro through one of the two methods referred to, was well-known at the time. Indeed, it was common knowledge amongst those skilled in the art that the same result could be achieved in at least five ways. Hence rapid dissolution by these two methods could never have been understood by those skilled in the art to constitute the 'surprising finds'. What the 'detailed disclosure' teaches at the outset, as I said, is that DSP is (a) sparingly soluble in water and at the same time, (b) unstable in an acidic environment, in that it rearranges into an inactive isomer in these conditions (ie that DSP is acid labile). It then continues to explain that – despite (b) – it has surprisingly been found that when DSP is provided in a rapidly dissolving form (which would ordinarily mean that both the solubility and the risk of degradation as a result of acid lability, were increased) high bioavailability was nonetheless attained in vivo. To the skilled operator, the 'surprising find' described would therefore be, in my view, the invention described by Prof Davies, which indeed came as a surprise to Bayer's development team. It is true that all this is not explicitly stated in the specification and that no mention is made, for instance, of enteric coatings. But as appears from the authorities I have referred to at the outset, one must read the specification through the eyes of a person skilled in the field and avoid the undue focus on a literal analysis in which lawyers tend to indulge.

[32] As I read it, there is therefore no basis upon which the limitation proposed by Pharma can conceivably be read into the claim of the patent in the context of the specification. On the contrary, I think the plain meaning of the claim read with the specification goes the other way. First of all it teaches that DSP can be provided in

micronised form or 'instead' that 'it is possible' for the dissolution rate of integer E to be achieved through the use of inert carrier particles. These are not statements from which one could infer that the claim should be limited to a particular method of achieving a dissolution rate. But what settles the matter, I think, is the patentee's express statement that 'composition of the invention may be formulated in any manner known in the pharmaceutical art'. This means that the composition of the invention could be formulated in any known manner that would achieve the dissolution rate specified in integer E, which includes the method employed in the formulation of Pharma's Ruby product.

[33] In sum I therefore agree with the court a quo's finding that the skilled reader of the patent (reading it as a whole) would accept that claim 1 covers any method of achieving the dissolution rate of integer E; that Pharma's Ruby product therefore falls within the compass of the claim and consequently infringes the 2004 patent.

Inventive step

[34] This brings me to Pharma's attack against the patent on the basis that it lacked an inventive step. The challenge must of course be understood in the light of s 25(10) of the Act which requires that, in order to be patentable, an invention must 'involve an inventive step' in the sense that 'it is not obvious to a person skilled in the art, having regard to any matter which forms, immediately before the priority date of the invention, part of the state of the art . . .' As explained by Plewman JA in *Ensign-Bickford (South Africa) (Pty) Ltd & others v AECI Explosives and Chemicals Ltd* 1999 (1) SA 70 (SCA) at 80H-J, a structured approach to the alleged obviousness of an invention involves the following enquiry:

'Four steps are identified. They include or restate in part what has been said above but may be taken to conveniently list the inquiries to be made:

(1) What is the inventive step said to be involved in the patent in suit?

(2) What was, at the priority date, the state of the art (as statutorily defined) relevant to that step?

(3) In what respect does the step go beyond, or differ from, that state of the art?

(4) Having regard to such development or difference, would the taking of the step be obvious to the skilled man?'

[35] As we know by now, the inventive step of the patent in suit contended for by Bayer and supported by Prof Davies, lies in the surprising, counter-intuitive finding that DSP, despite being both acid labile and poorly soluble, can be administered in a low dosage (of 2 to 4 mg), having the rapid dissolution rate of claim 1 and yet give sufficiently good bioavailability in vivo to be effective. We also know by now that the answer to this contention, as presented by Dr Rue, was that the skilled formulator would have determined experimentally at an early stage of the development of the drug that, despite DSP being acid labile, it does not in fact degrade in vivo.

[36] According to Dr Rue his thesis was supported by the state of the art at the priority date which showed that in vivo tests were conducted, even with highly acid labile drugs. In this regard he relied in particular on an article by two Swedish scientists, A Pilbrant and C Cederberg 'Development of an oral formulation of omeprazole' (1985) 108 *Scand J Gastroenterol Suppl* which was published in 1985 (the Pilbrant article). The article relates to the development of an oral formulation of the drug, omeprazole, which is both poorly soluble and highly acid labile. The article reflects that the authors considered whether to use an immediate release formulation of omeprazole or an enteric coated one. As part of their research they conducted in vivo tests, using the drug in both protected and unprotected formulations. The result of these in vivo tests corresponded to what was foreshadowed by the in vitro experiments: more than half of the omeprazole in the uncoated dosage degraded in the stomach. Although the Pilbrant article supports Dr Rue in that it evinces the performance of in vivo tests on a drug known to be acid labile, the results of the Pilbrant tests published in the article teaches away from the use of an acid labile drug, like DSP, in uncoated form. If anything, the article would therefore, in my view, persuade the skilled formulator in August 1999 to use an enteric coating in preparing any formulation containing DSP.

[37] In addition to the Pilbrant article, Pharma sought to find support for Dr Rue's views in Bayer's own internal documents. Apart from the fact that these are not public documents and do not therefore form part of the 'state of the art' as defined in s 25(6) of the Act, I believe they in fact do not support Dr Rue's thesis. According to Dr Rue, these documents show that Bayer conducted an in vivo experiment with unprotected DSP as a matter of routine, albeit at a late stage of the development. But that is not how I understand the Bayer documents. On my understanding, Bayer first spent about four years in the development of DSP protected by an enteric coating before it did any in vivo tests. Secondly, the in vivo tests were then conducted not so much with the view to establish the bioavailability of uncoated DSP but for the purpose of establishing possible shortcomings in the enteric coating actually used, that the formulator team suspected of being inefficient. In any event, it was not done, as Dr Rue would have it, as a matter of routine. In this light, I think the 'inventor's story' reflected in the Bayer documents, was supportive of Prof Davies' views rather than those of Dr Rue.

[38] As to the third inquiry contemplated in *Ensign-Bickford*, it appears to be common cause that the development of DSP as an oral contraceptive without an enteric coating went beyond and was a step different from the state of the art at the priority date. Dr Rue's thesis is that it fails the obvious test on the fourth step of the *Ensign-Bickford* inquiry, in that the taking of this step would be obvious to the skilled formulator after in vivo testing, which would have been done as a matter of routine. However, in evaluating Dr Rue's views, I believe they fall foul of at least two well-established principles in assessing obviousness. The first is that one must guard against the dangers of hindsight or *ex post facto* explanation of the invention (see eg *Gentiruco AG v Firestone SA (Pty) Ltd* 1972 (1) SA 589 (A) at 660G; *Roman Roller CC & another v Speedmark Holdings (Pty) Ltd* 1996 (1) SA 405 (A) at 418I-J). It is all too easy after the event and with the brilliance of hindsight, to say that a skilled formulator would have arrived at the invention earlier by doing an in vivo test.

[39] The second principle relates to Dr Rue's view that it would have been 'obvious to try' uncoated DSP, as a matter of routine, in an in vivo test. The principle is, however, that before an invention will be found to be obvious on the 'obvious to try' basis, it must be established by expert evidence that those skilled in the art would have carried out a test that led to the invention, not only because it was the obvious thing to do, but also because they would consider that a reasonable possibility existed that the test might lead to a useful result (see eg *B-M Group (Pty) Ltd v Beecham Group Ltd* 1978 BP 373 (T) at 405A-C). In this case it seems that, in the light of the in vitro results, the in vivo experiment that eventually led to the unsuspected invention did not seem to have the slightest hope of success before it was actually done.

[40] But what I find most unappealing about Dr Rue's theory is that it lacks any form of logical underpinning. It makes no sense for a formulator to take the time to do in vitro acid stability tests, and then to ignore the results by proceeding to carry out what are very expensive and time-consuming clinical trials on humans. What his proposition amounts to is that the skilled formulator would have conducted in vivo bioavailability tests regardless of the fact that he or she had no expectation that the formulation would not degrade in the stomach and therefore to take a step which was strongly contra-indicated. Stated somewhat differently: that the skilled formulator would disregard the considerable costs, delays and risks associated with carrying out in vivo tests in circumstances where the formulator had no expectation whatsoever that the test might lead to any useful result.

[41] By contrast, I find the reasoning of Prof Davies far more persuasive in its logical progression. In the light of this evidence I agree with the court a quo's conclusion that Pharma had failed to establish its attack on the patent in suit based on obviousness. This conclusion is also supported by the principle acknowledged in English law, that an invention can lie in 'finding out that which those in the art thought ought not to be done, ought to be done' (*Dyson Technology Ltd v Samsung Gwangju Electronics Co Ltd* [2009] EWHC 55 (Pat) at 154) or as it was formulated

by Jacob LJ in a passage cited in *Buhler AG v FP Spomax SA* [2008] EWHC 823 (Ch) para 47:

'A patentee who contributes something new by showing that, contrary to the mistaken prejudice, the idea will work or is practical has shown something new. He has shown that an apparent "lion in the path" is merely a paper tiger. Then his contribution is novel and non-obvious and he deserves his patent.'

Lack of novelty

[42] This brings me to Pharma's further ground of attack against the 2004 patent, based on the proposition that it is not a true 'divisional' of the 2002 patent and that it therefore lacks novelty in the light of the disclosures made in the 2002 patent. This ground is to be understood against the background of s 37 of the Patents Act which provides:

'1. Where at any time after an application had been lodged at the patent office and before it is accepted, a fresh application is made in the prescribed manner by the same applicant in respect of part of the matter disclosed in the first-mentioned application, the registrar may, on application made to him in the prescribed manner before that application is accepted, direct that such fresh application be antedated to a date not earlier than the date on which the first-mentioned application was so lodged.

2. A patent granted on such fresh application shall not be revoked or invalidated on the ground only that the invention claimed in such fresh application is not new having regard to the matter disclosed in the first-mentioned application.'

[43] It is common cause that the application for the 2004 patent was filed under s 37 before the 2002 patent had been accepted. Likewise it is common cause that if it constituted a 'fresh application' as contemplated by the section, it would enjoy immunity against an attack based on the disclosure of the 2002 patent by virtue of s 37(2), but that if it was not, it would be open to that attack. Pharma's argument is that it was not a 'fresh application' properly so called.

[44] Bayer's first answer to the attack is that, since the 2004 patent was granted as a divisional patent by the Registrar of Patents under s 37 in the form it was

sought, Pharma's remedy was to seek the setting aside of that decision in a review application which it never did. In support of this argument Bayer pointed out that s 61 of the Act – which enumerates the grounds for the revocation of a patent – does not provide for the revocation of a patent on the basis that it was wrongly registered as a 'divisional patent' under s 37. In further support of this argument, Bayer relied on the following statement by this court in *Clipsal Australia (Pty) Ltd & another v Trust Electrical Wholesalers & another* 2009 (3) SA 292 (SCA) para 9, which was made with reference to an analogous attack on the registration of a 'set of articles' in terms of the Designs Act 195 of 1993:

'If the registrar has registered articles as a set when they in truth do not form a set it is at best a matter for review but it cannot be raised as a defence to infringement or be a ground for revocation.'

[45] I believe Bayer's objection to be well-founded. At the same time I hold the view that Pharma's attack falls down on its merits as well. The procedure provided for in s 37 is referred to in patent parlance as 'dividing out' part of the matter disclosed in the parent patent as a divisional patent. The divisional patent is antedated and runs for the same period as the parent patent and claims priority from the same date. Ultimately, the two separate patents (the parent and the divisional) run in parallel and for the same length of time.

[46] The advantages of and requirements for divisional patents are explained with remarkable clarity by Jacob LJ in *Napp Pharmaceutical Holdings Ltd v Ratiopharm GmbH* and *Napp Pharmaceutical Holdings Ltd v Sandoz Ltd* [2009] EWCA Civ 252 paras 7-15. With regard to the requirements for a divisional patent he inter alia said:

'The two patents have, for practical purposes, the same text because they are "divisionals". The differences lie in their respective claims, and in variations of the text consequential upon the dividing out process.'

And:

'So what a patentee can do, having made an initial application, is to apply for a divisional patent. Provided the subject-matter of this does not extend beyond the content of the earlier application, he can get a free-standing patent for the divisional application. Because the

date of filing is deemed to be that of the "parent" as the jargon goes, a patentee cannot extend the period of protection by applying for a divisional.'

And:

'One of the features of the divisional system is that each divisional must have claims which are different: the patentee cannot have the same claim in different patents.'

[47] Pharma's first argument as to why the 2004 divisional application was not a divisional patent as contemplated in s 37 was that for all intents and purposes the body of the 2004 patent and that of the 2002 patent is the same. As a matter of fact, that is so. But, I do not think that renders the objection valid. As explained by Jacob LJ, the very idea of a divisional patent is that it has for practical purposes the same text as the parent. The invention disclosed is the same. The difference between the two lies in the claim.

[48] Pharma's second argument rests on the proposition that the claim of the 2004 patent is the same as the claim of the 2002 parent claim. Or, stated in patent law jargon, that the two claims are coterminous. As a matter of law, this cannot happen. That much appears, for instance, from the passage in the *Napp* case to which I have referred (see also T D Burrell *South African Patent and Design Law* 3 ed (1999) para 2.62). But this time the argument falls down on the facts. Claim 1 of the 2002 patent is expressly limited to DSP in micronised form. On the interpretation of claim 1 of the 2004 patent, contended for by Pharma, the two would indeed be the same. But I have already held that interpretation unsustainable. In accordance with the contrary interpretation of the 2004 claim contended for by Bayer – which I found to be correct – this claim is broader than the 2002 parent claim, in that it includes DSP having the rapid dissolution rate specified in the claim, however that dissolution rate had been obtained, which clearly includes, but is not confined to micronisation. This means that the two claims are not coterminous. Following upon this, Pharma's further argument was that s 37 does not allow a divisional claim which is broader than the parent claim. It sought to find support for this argument in the statement by Jacobs LJ in *Napp* (para 10) that 'Provided the subject matter of this [ie the divisional patent]

does not extend beyond the content of the earlier [parent] application, he can get a free-standing patent for the divisional application'. But I do not believe that this statement lends support to Pharma's argument. What Jacob LJ refers to is that the claim of the divisional patent cannot be broader than the invention disclosed in the body of the parent patent. This would, after all, give rise to a ground of revocation that the claim is not fairly based on the matter disclosed in the application (see s 61(f)(ii) of the Act).

[49] Pharma's final argument as to why s 37 should be construed so as to exclude a divisional patent which claims broader protection than its parent, is that it could otherwise place the infringer of both patents in an invidious position when licences in respect of the two patents were granted to different licensees. In this event, so Pharma's argument went, the infringer could potentially be held liable by two plaintiffs instead of one. I believe there are two answers to this argument. First, I do not think the position would be any different if the divisional patent is narrower than the parent. Secondly, the prejudice feared by Pharma seems to be more apparent than real. If the remedy sought by the two licensees is an interdict, the two interdicts will clearly overlap. If on the other hand, the remedy sought is one in the form of damages, each licensee will be confined to the amount that he or she can establish. In the circumstances, I find that Pharma's attack of the patent on the basis of novelty must also fail.

Conclusion

[50] For these reasons the appeal is dismissed with costs, including the costs of two counsel.

_____
F D J BRAND
JUDGE OF APPEAL

APPEARANCES:

For the Appellant:	L Bowman SC and B du Plessis Instructed by: Von Seidels, Cape Town c/o Webbers, Bloemfontein
For the Respondent:	P Ginsburg SC and G Marriott Instructed by: Adams & Adams Inc, Pretoria c/o Honey Attorneys Inc, Bloemfontein