Merck & Co, Inc v Pharmaforte Singapore Pte Ltd
[2000] SGCA 39

Case Number : CA 9/2000

Decision Date : 28 July 2000

Tribunal/Court : Court of Appeal

Coram : Chao Hick Tin JA; L P Thean JA; Yong Pung How CJ

Counsel Name(s) : P Sivakumar and Vicki Heng (Ella Cheong & G Mirandah) for the appellants; Ranvir Kumar Singh and Vivienne Kaur (Kumar & Loh) for the respondents

Parties : Merck & Co, Inc — Pharmaforte Singapore Pte Ltd

Patents and Inventions – Infringement – Validity of patent

Patents and Inventions – Novelty – Lack of utility in invention – Registered patent comprising Lovastatin – Allegation that Apo-Lovastatin infringes patent comprising Lovastatin – Definition of "utility" – Whether lack of utility renders invention unpatentable for want of novelty – Whether differences in degree of compound patentable – Whether invention anticipated by prior art

Patents and Inventions – Inventive step – Whether invention obvious to person skilled in the art – Whether mere discovery patentable – Whether person skilled in the art could use existing standard techniques to purify Lovastatin

(delivering the judgment of the court):This is an appeal against the decision of Lai Kew Chai J where he dismissed the appellant`s claim against the respondents for patent infringement and held that the products claims in claims Nos 16-21 of the patent in suit are invalid. He also held that the process which the respondents adopted to manufacture their product was different from the process disclosed in claim No 11.

The appellants are one of the largest pharmaceutical companies in the world. They are the registered proprietors of Singapore Patent No 9690405-7 (registered on 15 June 1996), the patent in suit, which relates to a `process for the lactonization of mevinic acids and analogs thereof.` This patent, which comprises both process (lactonization) and product (Lovastatin with a dimeric impurity of less than 0.2%) claims, is derived from the European Patent No 0351918B1 (filed on 17 July 1989 and granted on 14 September 1994) and which in turn claimed priority from the US Patent application No 221475 filed on 19 July 1988 (the priority date).

The respondents are a Singapore incorporated company that import and distribute pharmaceutical products, including a product called `Apo-Lovastatin` which is manufactured in Canada by Apotex Inc, the largest pharmaceutical company in that country. It was the importation of the product, `Apo-Lovastatin`, which gave rise to this action.

The facts

In June 1979 the appellants filed patent applications in the United States and elsewhere on the compound Lovastatin and certain fermentation processes which they had been developing to produce the compound. In that patent, the appellants claimed that their cultivation of a micro-fungus of the genus Aspergillus produced a new compound that was a potent inhibitor of the biosynthesis of cholesterol in humans. The compounds of that invention were useful as anti-hypercholesteremic agents for the treatment of atherosclerosis, hyperlipernia and similar diseases in humans. Those compounds are collectively termed `statins`. Statins are marketed in a form known as the `lactone form`. The lactone is a chemical ring structure and is obtained from the free acid formed by the

process of `lactonization`. The process of lactonization results in lactone forming from an intramolecular condensation of the free acid. However, an intermolecular condensation of a pre-formed lactone with another open acid molecule leads to the formation of an inactive dimer. In the past, it was thought that the formation of such dimers could not be completely suppressed. Therefore, dimer impurity in statins in amounts from 0.4 - 0.8% was deemed to be unavoidable.

The patent in this suit, as mentioned above, was first filed in the United States on 19 July 1988. That patent contained claims for a compound made by a specific process which minimize the formation of the dimer impurity when the compound Lovastatin is converted from its open acid form into a lactone form. However, that US patent did not contain a stand-alone product claim. About a year later, on 17 July 1989, the appellants filed an European patent application, claiming priority from the US filing date. The European patent application contained stand-alone product claims to the compound Lovastatin where the dimeric impurity was at a level of less than 0.2%, regardless of the method of manufacture.

This action was instituted by the appellants because they claimed that the product, Apo-Lovastatin, manufactured by Apotex Inc of Canada and imported into Singapore by the respondents possessed dimeric impurity levels of less than 0.2%, and infringed their patent rights. Specifically, they alleged that the respondents have infringed claims 16-21 (the product claims) and claim 11 (the process claim).

The respondents argued that the product claims are invalid because they lack novelty and an inventive step. As regards the process claim, the respondents contended that the process employed by Apotex Inc to produce Apo-Lovastatin was different from the process specified in claim 11. The trial judge upheld all the contentions of the respondents. In coming to the conclusion that the patent was invalid, he found that the appellants` product was not novel. He held that utility is an essential requirement of novelty, and, in this instance there was an absence of utility. He also found that the patent in suit had been anticipated by prior disclosures. He further held that differences in degree of purity of a compound were not patentable, as opposed to differences in the type or kind of compound. As regards the requirement of an inventive step, the trial judge held that the purification of Lovastatin was an obvious step for a person skilled in the art to take.

The appeal

In his submission before us, counsel for the appellants did not pursue the point relating to the process claim as he recognised that that point related to a finding of fact. However, counsel contended that the trial judge was wrong in his findings on both the novelty point as well as the inventive step point.

Utility

The first line of attack of the appellants concerns the element of utility. Counsel submitted that the trial judge erred when he relied upon the irrelevant issue of utility, raised by the respondents, to arrive at his decision that the product claims were invalid. We will now quote what the trial judge said (at [para] 23):

> *... a more useful prescriptive test particularly for cases of this kind, within a novelty enquiry, is an assessment of the utility of the patented product. There are no shortage of cases which clearly impose the requirement of utility as a necessary ingredient of patentability notwithstanding its absence as a statutory requirement of novelty.*

At this juncture, it is necessary for us to quote the relevant provisions of our Patents Act 1994, which are based on the English Patents Act of 1977:

> *13(1) Subject to subsections (2) and (3), a patentable invention is one that satisfies the following conditions:*
>
> *(a) the invention is new;*
>
> *(b) it involves an inventive step; and*
>
> *(c) it is capable of industrial application.*
>
> *80(1) Subject to the provisions of this Act, the Registrar may, on the application of any person, by order revoke a patent for an invention on (but only on) any of the following grounds:*
>
> *(a) the invention is not a patentable invention:*

Under the previous UK law, the Patents Act 1949, a patent could be revoked where [s 32(1)(g)]:

> *the invention, so far claimed in any claim of the complete specification, is not useful.*

In view of the absence of s 32(1)(g) in the 1977 Act (and in our 1994 Patents Act), the appellant argued that `utility` is no more a prerequisite to acquiring a patent under s 13.

The appellants contended that the 1994 Act establishes a completely new code for patents and that it is no longer necessary to establish utility. In this regard, they relied upon **Genentech Inc`s Patent** [1989] RPC 147 where Purchas LJ explained that the 1977 Act:

> *provided a complete code dealing with the application for and grant of a patent and thus displaced any residual common law element which previously had been preserved by succeeding statutes.*

In **Unilever Ltd (Davis`s) Application** [1983] RPC 219 Falconer J (at p 229), in answer to the argument that in the absence of clear wording the legislature must be presumed not to have intended to change the law, said:

> *Parliament made it abundantly clear in the long title to the Act ... that the old law of patents is being swept away.*

Basing on the above, counsel for the appellants submitted that what is provided in the 1994 Act is exhaustive and that the earlier English decisions, which viewed the utility of a product to be a

relevant factor in the assessment of novelty, and thus patentability, should not be relied upon, it being something swept away by the new law.

We must, however, point out that `inutility` as a ground to revoke a patent was only introduced in the 1949 UK Act. The Patents Act before 1949 did not contain such a provision. Before then, the absence of a provision similar to s 32(1)(g), had never precluded the court from considering the question of `utility` in determining patentability. In **Badische Anilin Und Soda Fabrik v Levinstein** [1887] 4 RPC 449, the Lord Chancellor expressly addressed the point when he stated (at p 462):

> *there is certainly authority for saying that an invention must be useful, although that word is not found in the statute ... but it is obvious.*

In **Welsbach Incandescent Gas Light Co Ltd v New Incandescent (Sunlight Patent) Gas Lighting Co Ltd** [1900] 17 RPC 237 the court said:

> *Utility, in Patent law, does not, as I understand it, mean either abstract utility, or comparative or competitive utility, or commercial utility. It was described by Mr Justice Grare, in Young v Raseulled, in 1st Reports of Patent Cases, page 34, as meaning an invention better than the preceding knowledge of the trade as to a particular fabric. I adopt this definition if the word `better` be understood as meaning better in some respects and not necessarily better in every respect; so that, for instance, an article which is good, though not so good as that previously known, but which can be produced more cheaply by another process, is better in that it is better in point of cost, although not so good in point of quality.*

At this point it may perhaps be appropriate to refer to the sense in which the respondents are contending that there is a lack of utility in the subject invention. What the respondents are saying is that Lovastatin with a dimer impurity of less than 0.2% does not have any improved performance or therapautic advantage as compared with existing statins, as an anti-hypercholesteremic agent in the treatment of atherosclerosis, hyperlipemia and like diseases. Lai Kew Chai J ruled that utility was relevant in the assessment of novelty, and thus patentability, of an invention and as the compound Lovastatin with less than 0.2% dimer impurity lacked utility in that sense, it was not patentable.

However, it seems to us, that what is important is to determine the meaning common law attributed to `utility` before 1949. On this, the following passage of Parker J in **Alsop`s Patent** [1907] 24 RPC 733 is pertinent:

> *In considering the validity of a patent for a process it is, therefore material to ascertain precisely what the patentee claims to be the result of the process for which the patent has been granted; the real consideration for which he gives for the grant is the disclosure of a process which produces a result, and not the disclosure of a process which may or may not produce any result at all. If the patentee claims protection for a process for producing a result and that result cannot be produced by the process, in my opinion the consideration fails. Similarly, if the patentee claims a process producing two results combined and only one of these results is in fact produced by the process, there is a partial failure of consideration ... and such partial failure of consideration is sufficient to avoid the patent ... Objections to patents on [this ground] are sometimes treated as objections for want of utility, and when so treated the well known rule is that the utility of an invention depends upon, whether by following the directions of the patentee, the result which the patentee professed to produce*

> *can in fact be produced. Want of utility in this sense must be distinguished from want of utility in the sense of the invention being useless for any purpose whatsoever. In the case of an invention not serving any useful purpose at all, the patent would no doubt be void, but not entirely for the same reason. It would probably be void at common law on the ground that the King`s prerogative could not be properly exercised unless there were some consideration moving to the public, and the public could not be benefited by the disclosure of something absolutely useless.*

Earlier in **Lane Fox v Kensington & Knightsbridge Electric Lighting Co Ltd** [1892] 3 Ch 431 Lindley LJ said:

> *The utility of the alleged invention depends ... on whether by [directions in the complete specification] the effects which the patentee professed to produce could be produced ... Utility is often a question of degree, and always has reference to some object. Useful for what? is a question which must be always asked and the answer must be, useful for the purposes indicated by the patentee.*

As the 1977 Act (and our 1994 Act) does not contain a provision similar to s 32(1)(g), we are really thrown back to the position pre-1949. There is nothing to suggest that the patent in suit could not produce Lovastatin with a dimer impurity of less than 0.2%. The fact that this compound, Lovastatin, with a lessor dimer impurity, is of the same efficacy as a statin with a higher degree of dimer impurity does not, therefore, render it of no utility. Some of the older cases would seem to indicate that for an invention to be patentable there must be new use or further advantages. An example is **Lawrence v Perry & Co (Ltd)** [1884] 2 RPC 179 where North J said (at p 184): `I have felt some difficulty in seeing how the plaintiff`s invention can be useful if it only differs from an earlier one by an ingredient which does neither harm nor good.` As we see it, the argument on this should be more appropriately subsumed under the investigations whether the invention is anticipated by prior art or whether it involved an inventive step. This was the approach taken in **Merrell Dow Pharmaceuticals Inc & Ors v HN Norton & Co Ltd** [1996] RPC 76 to which we will refer to later.

Difference in purity

We now turn to the next issue raised by the appellants, namely, whether the trial judge is correct to have accepted the respondents` submission, that differences in degree of a compound are not patentable, only differences in the kind of the compound are. He held because of this, the product claims lack novelty. On this question he relied strongly on the case **Farbenfabriken vormals Friedrich Bayer & Co v Chemische Fabrik Von Heydon** [1905] 22 RPC 501 (the Bayer case).

The appellants contend that the trial judge is wrong to have found that the ratio of the case established that proposition. ***Bayer*** was concerned with the common drug called `aspirin` whose scientific name is `acetyl salicyclic acid` and the patent owner there claimed that their product, aspirin, was a new product because it was in purer form. Prior art showed that acetyl salicyclic acid could be obtained by chemical reaction between salicyclic acid and acetyl chloride. The resulting crystals of acetyl salicyclic acid could be purified by recrystallization. The plaintiff obtained a patent for acetyl salicyclic acid as a new body or compound. However, the claim was rejected by Joyce J who said (at p 515):

> *the patent is claimed for a body or product the name of which was known, the characteristic and properties of which had been described with more or less accuracy and a method of getting it had been published. There was no novel idea in the patent.*

In ***Bayer*** , the product and the impurity were known entities at the time the patent application was filed. That is unlike the present case where Lovastatin with less than 0.2% of dimer impurity had not yet been produced and knowledge of the dimer impurity was not part of the common knowledge of the skilled addressee. As on the priority date, not all the impurities in Lovastatin had been discovered.

It seems to us clear that in ***Bayer*** , the patent was for aspirin as a new product and which product had previously been produced in its pure form and the patent owners had relied on a method that was known and obvious, recrystallization method, to produce it. It seems to us that the patent in Bayer was invalidated due to both lack of novelty and lack of an inventive step. Accordingly, we agree with the appellants that ***Bayer*** does not stand for the proposition that mere differences in the degree of a compound are not patentable.

Indeed, there are cases which indicated that a purer form of a known product is patentable. In **Badische Anilin Und Soda Fabrik v Societe Chimique des Usines Du Rhone & Wilson** [1898] 14 RPC 875 (` ***Badische Anilin*** `) the plaintiffs` patent of pure anisoline was upheld. Wills J said (p 887):

> *The plaintiffs` product is pure anisoline, and pure ansoline seems to me, to be a substantially different product from anisoline with either 30 per cent or 18 per cent of foreign matter.*

The court there clearly thought that purity was a very important element in the worth of a product and thus a purer version could in itself be sufficient to ward off a challenge of anticipation or lack of novelty. In fact, in Badische Anilin it was thought that the anisoline product produced by the prior act was pure, when it was not, as the presence of impurities was not realized.

In **Joseph Lucas (Batteries) Ltd & Anor v Gaedor Ltd & Ors** [1978] RPC 297 which was concerned with a patent in relation to cases for the storage batteries of the kind suitable for use in moving vehicles, eg cars and lorries, the prior art had cases for the storage of batteries with walls and bottom of average thickness in excess of 0.2 inch. The patentee invented a case with side walls, bottom and partitions of a thickness not in excess of 0.1 inch, and the case having a cover in the form of a single moulded polypropylene unit. Both the objections of lack of novelty and lack of an inventive step were raised and both failed. The court recognised that the invention was an improvement over previous batteries cases which had a wall thickness averaging about 0.2 of an inch. Although there were prior battery cases made of polystyrene which had walls of 0.12 and 0.13 inch thickness, that did not preclude the patentee`s patent from being novel. In response to the point that the reduction of the thickness was something obvious and that there was no inventive step, Whitford J said:

> *I confess quite freely that when this case was opened to me I felt the gravest doubts as to whether a claim to this dimensional limitation could possibly stand good. What was done in practice by so many experts on the evidence before me has indeed convinced me that the step taken leading to a battery with walls as thin as 0.10 or less was not an obvious one.*

The respondents sought to argue that ***Joseph Lucas*** involved a reduction in the thickness of battery cell walls leading to recognised commercial benefits. In contrast, in our case, the dimeric impurity is a harmless substance and its reduction would not change the compound`s therapeutic properties. Still, we do not see how a purer form of Lovastatin can be anything other than commercially more desirable. Even Dr Barrett, the appellants` expert, a professor in Chemistry from Imperial College, London, said in his affidavit of evidence-in-chief that `lactone containing higher levels of impurities is clearly much less desirable for use in medicines as antihypercholesterolemic agents.`

Counsel for the appellants also drew our attention to a US case and a European Patent office (EPO) case which held that a purer form of a known substance could be patentable. The US case is **Application of Sune Bergstrom and Jan Sjovall** [1970] 427 F 2d 1394 where the US Court of Customs and Patent Appeals held, though the purer form was not of therapeutic advantage:

> *We need not decide the merits of that matter, for the fundamental error in the board`s position, as we see it, is the analysis and answer it gave to the sole issue it accurately posed - `whether the claimed pure materials are novel as compared with the less pure materials of the reference`. It seems to us that the answer to that question is self-evident: by definition, pure materials necessarily differ from less pure or impure materials and, if the latter are the only ones existing and available as a standard of reference, as seems to be the situation here, perforce the `pure` materials are `new` with respect to them.*
>
> *...*
>
> *Moreover, whether the claimed pure materials have the same usefulness or assortment of properties as the impure materials of the prior art, as the board here found, is a question having no bearing on the factual and legal matter whether pure materials are new vis-Ã -vis impure materials within the meaning of s 101, although it is but one of the factors to be considered in determining their obviousness under 35 USC 103.*

In that case the court left open the question if such a new compound was unpatentable for lack of inventive step, ie obviousness.

The EPO`s case is **Toshiba/Thickness of Magnetic Layers** [1990] EPOR 267. There, there was already a recording medium with a recording layer of a thickness from 0.1 UM to 3 UM. The Technical Board of Appeal allowed a claim where the thickness of the magnetic recording layer was in the range between 0.05 UM and 0.1 UM. It stated:

> *In the present case, therefore, there exists in the prior art a reasoned statement clearly dissuading the person skilled in the art from using in a double layer medium a thickness of the recording layer below 0.1 UM. In the light of the reasoning set out above, the Board is of the opinion that the range of thickness values below 0.1 UM and in particular the range 0.05-0.1 UM has to be regarded as novel.*

The above cases illustrate that a purer form of a known compound or a dimensional limitation of a known product could be novel and patentable. But really, like the first issue of `utility`, we do not think it is a profitable exercise to inquire whether a purer form of a known compound or a dimensional

limitation of a known product is per se patentable. Firstly, we do not think we should generalise bearing in mind that there are so many kinds or types of invention and their circumstances are different. Second, in the light of the modern law as set out in the UK 1977 Act (and our 1994 Act) where for the first time the statute prescribes the criteria for patentability, this issue should not be considered in isolation but in the context of whether the invention has been anticipated by prior art or lacks an inventive step. This latter point is really the question to pursue.

Existing state of this art

We now turn to the point about `novelty` where the learned trial judge found that the invention had been anticipated by prior disclosure. Sections 14(1) and (2) of our Act provides as follows:

> *(1) An invention shall be taken to be new if it does not form part of 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 Singapore or elsewhere) by written or oral description, by use or in any other way.*

Thus prior disclosures would render an invention non-patentable. The state of the art as on the priority date is therefore crucial. On this question, the respondents relied upon two Canadian patents issued to the appellants before the priority date. First is patent No 1,199,322 (CP 322), issued to the appellants on 14 January 1986, and entitled `Antchypercholesterolemic Compounds` and which described a process of purification which the appellants had followed after lactonization. It referred to the use of decolourizing charcoal (activated carbon) to the crude solid. It did not specify the amount of charcoal to be used but suggested that 1-2% by weight of decolouring charcoal to the crude solid would be sufficient. Neither did it specify the amount of time necessary for the solution to be filtered through the charcoal. Second is patent No 1,161,380 (CP 380), filed on 11 June 1980 and issued on 1 January 1986, where the appellants disclosed how they were able to separate the hydroxy acid from Lovastatin through the use of the APLC technique.

Based on the teachings set out in CP 322, Dr Sailer, the Chemistry Lab Leader and a Downstream Process Scientist at Apotex Inc, Canada, conducted various experiments. In his report, Dr Sailer stated that two of the four activated carbons experimented (Darco G-60 and Calgon F-400) reduced the dimer impurity level of the compound from 0.27% to 0.05% and 0.16% respectively. Darco G-60 had been available for over 30 years and Calgon F-400 since 1974.

The appellants challenged the veracity of these experiments and pointed out three aspects to show that Dr Sailer did not quite follow the teachings in CP 322. First, contrary to the teachings in CP 322, Dr Sailer had used an unusually large quantity of charcoal, 50% by weight of charcoal to the crude solid, when the common practice and that specified in the teachings was only 1-2%. Because of the use of a much greater amount of charcoal, more Lovastatin was absorbed leading to results which appeared to show that the dimer impurity had been substantially reduced. Second, there is a flaw in the results of Dr Sailer`s experiments in that the figures obtained by Dr Sailer were by measuring the ratio of the dimer to the Lovastatin as opposed to calculating the absolute values of the dimer. Third, Dr Sailer agitated the solution with the charcoal for one hour, which was not a procedure suggested

in CP 322.

Dr Sailer also carried out another experiment, following the teachings of CP 322, this time using crude Lovastatin with a dimer content of 0.54% and where he dissolved the crude Lovastatin in hot ethyl acetate and treated it with Calgon F-400 for two hours. After filtration and concentration, Lovastatin was crystallised from the concentrated ethyl acetate solution. After one carbon treatment of the hot acethyl solution, the concentration of Lovastatin dimer was reduced from 0.54% to 0.3%. A single recrystallization from acethyl acetate further reduced the Lovastatin dimer from 0.3% to 0.17%. The appellants contended that this said single recrystallization technique used by Dr Sailer was an exact replication of the process covered by the patent in suit. But Dr Sailer said that he simply followed the instructions laid down in CP 322 and obtained a dimer level of 0.17%.

As regards CP 380, Dr McClelland, a professor in Chemistry at the University of Toronto and an expert called by the respondents, said that by the use of the HPLC method, which is a method available from the early 1970s, one would be able to separate the dimer from the crude Lovastatin. While the appellants accepted that the HPLC method was available as from early eighties (not seventies), they contended that it could not be used in large-scale preparations of organic pharmaceuticals, since that method could only yield minute quantities of pure compound at any one time. In short, one cannot use HPLC as a method to manufacture the pure form of Lovastatin on a large commercial scale.

In **General Tire & Rubber Co v Firestone Tyre & Rubber Co Ltd & Ors** [1972] RPC 457 the Court of Appeal set out the approach a court should take when considering the issue of prior disclosure by publication, in these terms (at p 485):

> *When the prior inventor`s publication and the patentee`s claim have respectively been construed by the court in the light of all properly admissible evidence as to technical matters, the meaning of words and expressions used in the art and so forth, the question whether the patentee`s claim is new for the purposes of section 32(1)(e) falls to be decided as a question of fact.* ***If the prior inventor`s publication contains a clear description of, or clear instructions to do or make, something that would infringe the patentee`s claim if carried out after the grant of the patentee`s patent, the patentee`s claim will have been shown to lack the necessary novelty, that is to say, it will have been anticipated****. The prior inventor, however, and the patentee may have approached the same device from different starting points and may for this reason, or it may be for other reasons, have so described their devices that it cannot be immediately discerned from a reading of the language which they have respectively used that they have discovered in truth the same device; but if carrying out the directions contained in the prior inventor`s publication will inevitably result in something being made or done which, if the patentee`s patent were valid, would constitute an infringement of the patentee`s claim, this circumstance demonstrates that the patentee`s claim has in fact been anticipated.*
>
> *If, on the other hand, the prior publication contains a direction which is capable of being carried out in a manner which would infringe the patentee`s claim, but would be at least as likely to be carried out in a way which would not do so, the patentee`s claim will not have been anticipated, although it may fail on the ground of obviousness.* ***To anticipate the patentee`s claim the prior publication must contain clear and unmistakeable directions to do what the patentee claims to have invented****: **Flour Oxidizing Co Ltd v Carr & Co Ltd** ((1908) 25 RPC 428 at 457, line 34, approved in **BTH Co Ltd v Metropolitan Vickers Electrical Co Ltd** [1928] 45 RPC 1 at 24, line 1). A signpost, however clear, upon the road to the patentee`s invention will not suffice. The prior inventor must be clearly shown to have planted his flag at the precise*

destination before the patentee. [Emphasis added.]

In ***Merrell Dow*** (supra) a similar point came up for consideration by the House of Lords. There the plaintiffs discovered an anti-histamine drug called terfenadine for use by people who suffered from hay-fever and similar allergies. Unlike other similar drugs, this drug did not have the side effect of making the person drowsy. The plaintiffs` exclusive right to terfenadine expired in December 1992. Other drug manufacturers thus embarked on making and marketing terfenadine. However, the plaintiffs claimed that their monopoly in terfenadine continued because of a later patent. This later patent came about because their research showed that terfenadine was absorbed in the small intestines and was then 99.5% metabolised in the liver. This was why it had no side effects. They analysed the chemical composition of the acid metabolite formed in the liver. No one had identified that compound before. So they patented the acid metabolite. The plaintiffs` claim to a later patent was in respect of acid metabolite as a product. The defendants contended that while acid metabolite as a chemical compound had not been previously identified, its manufacture in the body by the ingestion of terfenadine was nevertheless part of the state of the art. This submission was upheld by the House, which essentially approved the approach taken in ***General Tire*** . Lord Hoffmann, who delivered the only judgment of the House, said:

> *Anticipation by disclosure, on the other hand, relies upon the communication to the public of information which enables it to do an act having the inevitable consequence of making the acid metabolite. The terfenadine specification teaches that the ingestion of terfenadine will produce a chemical reaction in the body and for the purpose of working the invention in this form, this is a sufficient description of the making of the acid metabolite. Under the description, the acid metabolite was part of the state of the art.*

Adopting the test laid down in ***General Tire and Merrell Dow*** it seems to us that for CP 322 and CP 380 to have anticipated the patent in suit, it must be established that by following the teachings in those two patents it would inevitably lead to the production of Lovastatin with less than 0.2% demeric impurity. As mentioned above, Dr Sailer, in carrying out the experiments, had used a much larger quantity of charcoal and had agitated the solution instead of just filtering it. In short, he did not exactly follow the teachings. He modified the experimental environment. Thus, the experiments of Dr Sailer cannot be relied upon to show that following the teachings of CP 322 would inevitably have the consequence of producing Lovastatin with a dimer impurity of less than 0.2% because he had made modifications.

As regards CP 380, all that the respondents were able to tender to court was an opinion of Dr McClelland. There was no cogent evidence that Lovastatin with a dimer impurity of less than 0.2% would inevitably be produced upon employing the HPLC technique. Dr McClelland did not carry out any specific experiment using the HPLC technique. He admitted as much that his conclusion was extrapolated from the prior art documents and was therefore in a sense speculative. Although there is a HPLC chromatogram prepared by the appellants on 16 March 1986 which shows that the appellants were able to separate the dimer from the hydroxy acid and other contaminants, it nowhere shows that the Lovastatin produced would be a compound with less than 0.2% of dimeric impurity.

In the light of the foregoing, we do not think that the test as to prior art is satisfied in this instance. The respondents, upon whom the burden rest, had failed to discharge it. Thus, it is our opinion that Lovastatin with a dimer level of less than 0.2% had not been anticipated by the two Canadian patents or any other prior art.

We recognise that there are some apparent similarities between ***Merrell Dow*** and the present case. First, in ***Merrell Dow*** the argument taken was that no information had been made available to the public about the metabolite before the priority date, very similar to the position taken here by the appellants that they had kept the existence of the dimer confidential before the priority date. Second, in ***Merrell Dow*** it was also alleged that no one was aware that the product was being made, similar to that asserted here by the appellants that the respondents did not know about the dimer. But these are not the crucial factors which differentiate the present case from those of ***Merrell*** , where the House of Lords held that there was prior disclosure. Here, it has not been shown that following the teachings of the two Canadian patents would have the inevitable consequence of producing Lovastatin with dimeric content of less than 0.2%. On the other hand, in ***Merrell Dow*** , the specifications of terfenadine had taught the public that the ingestion of terfenadine would produce a chemical reaction in the body, and that led to the formation of a chemical compound. That, the House held, was a `sufficient description of the making of the acid metabolite`, and thus the acid metabolite was part of the state of the art.

Inventive step

Section 15 of our Patents Act provides that `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 14(2) and without having regard to section 14(3).`

In his judgment the learned trial judge held that a skilled addressee would, based on the prior art disclosures, have been instructed to make Lovastatin with a dimer impurity of less than 0.2%.

(i) Appellants` contentions

The appellants emphasised that they were the only pharmaceutical company in the world that worked on statins as a means of lowering cholesterol. The first time dimer impurity was ever mentioned was in the appellants` patent in suit. They pointed out that the trial judge made an error when he said that the prior art did not make specific reference to a dimeric impurity level of 0.2% or less. The truth was that the prior art made no reference to dimeric impurity at all. No other company or research organisation was doing such similar work. A normal skilled addressee would not be aware of the existence of dimer impurities in statins. The prior publication of the two Canadian patents nowhere mentioned any dimer impurities. The respondents` witness, Dr Sailer, agreed that research and development to produce a compound like Lovastatin would take years. The appellants asked, is it likely that a skilled addressee would have, using the words of the trial judge, `clear and unmistakable directions to do what the patentee claims to have invented.`?

Counsels for the appellants emphasised that the test laid down in Merrell Dow to determine anticipation by disclosure is that the disclosure of the prior information must have the inevitable consequence of producing the invention in question. There is no evidence of any disclosure, relied upon by the respondents, which had the inevitable consequence of disclosing the invention, ie Lovastatin with a dimer impurity of less than 0.2%.

The appellants also explained that the monopoly claimed by them is no wider than that claimed by the plaintiffs in ***Joseph Lucas*** : so long as any third party should manufacture a battery storage case, from whatever method, from polyprepylene and had walls of a thickness of less than 0.1 of an inch, the third party would have infringed the patentee`s right. This principle was reaffirmed by Lord Hoffmann in ***Merrell Dow*** where he said `For this purpose it does not matter how the product is made

or what form it takes. The monopoly covers every method of and every form which comes within the description in the claim.`

Finally, the appellants argued that while the normally skilled addressee is expected to have the skill to make routine workshop development he is not expected to exercise inventive ingenuity. Further, the skilled man should not be expected to try all combinations unless he has a problem in mind and a particular combination might assist him in solving it. As of the priority date, there was no mention anywhere of dimer impurity in Lovastatin. In fact, from the material furnished by the respondent it was assumed, of course mistakenly, that pure Lovastatin had been produced. In such circumstances, the normally skilled addressee would have no reason to examine or addressed the question of reducing dimer impurity. There was no evidence that it was common knowledge to the skilled addressee that Lovastatin contained dimer impurity, let alone dimer impurity of between 0.4 to 0.8%.

The appellants also relied on the fact that Dr Sailer agreed that in the late seventies and in the eighties, the appellants were the only entity working on the dimer in the Lovastatin. When asked, would it mean that nobody else would have detected the dimer, Dr Sailer said (at CB 598):

> *If you don`t have lovastatin, and you don`t do lactonization, you cannot detect dimer. You must be the person who is working with the compound in large quantity. If there was some university group working on lovastatin, they perform usually with a small amount and they don`t look for impurity like a dimer. But the manufacturer of the drug should look for all impurities.*

(ii) Our determination

First, it is important to determine the approach which should be adopted to assess whether an invention involved an inventive step. Here, there is a very helpful passage of Oliver LJ in **Windsurfing International v Tabur Marine** [1985] RPC 59 where he enunciated four steps one should take (at p 73):

> *There are, we think, four steps which require to be taken in answering the jury question. The first is to identify the inventive concept embodied in the patent in suit. Thereafter, the court has to assume the mantle of the normally skilled but unimaginative addressee in the art at the priority date and to impute to him what was, at that date, common general knowledge in the art in question. The third step is to identify what, if any, differences exist between the matter cited as being `known or used` and the alleged invention. Finally, the court has to ask itself whether, viewed without any knowledge of the alleged invention, those differences constitute steps which would have been obvious to the skilled man or whether they require any degree of invention.*

Of course, in this exercise one must guard against any contention of obviousness which is based on the benefit of hindsight and on this Oliver LJ said (at p 71) that the question:

> *... has to be answered, not by looking with the benefit of hindsight at what is known now and what was known at the priority date and asking whether the former flows naturally and obviously from the latter, but by hypothesizing what would have been obvious at the priority date to a person skilled in the art to which the patent in suit relates.`*

The compound Lovastatin was first reported in an article in a scientific journal in August 1979 written by a Japanese scientist called Akira Endo. In July 1980, employees of the appellants published a paper describing the compound Lovastatin (also known then as Mevinolin).

In this regard, we have to return to the two Canadian patents obtained by the appellants - CP 322 and CP 380. They would be prior art. CP 322 teaches the use of decolourizing carbon in a purification step performed after the lactonization step. As mentioned before, Dr Sailer had performed experiments following the teachings of CP No 322 and they reduced the dimer impurity of the compound to that well below 0.2%. In fact he said within about 2-3 months he was able to use charcoal effectively to reduce the dimer impurity. On this basis the respondents contend that that constituted a prior act within the principle enunciated by Lord Hoffman in ***Merrell Dow*** :

> *If there is any method of manufacture or form of the product which is part of the state of the art, then to that extent, the invention is not new.*

There is also evidence that before the priority date there were available purification techniques, eg treatment by activated carbon, recrystallization and preparative HPLC. Dr Barrett admitted as much. The respondents` expert, Dr Robinson, a professor of Pharmaceutical Sciences and who has worked in the pharmaceutical industry for over 35 years, stated quite clearly:

> *the prior art of increasing the purity of pharmaceuticals, is many decades, if not centuries, old. Techniques to reduce the levels of impurities in a chemical such as through recrystallization, absorption to a high surface area solid such as charcoal, ion-exchange resin and various chromatographic approaches have been taught at the University and High-School level for many decades.*

He further explained that he had no difficulty projecting himself back to that period of time:

> *These techniques that have been available are decades, many decades old and the issue of not being able to run the full gamut of these to reduce the impurity doesn`t make any sense. There are many materials that are difficult to remove as impurities but there are a wide range of technologies available to reduce them and it`s a question of how much effort you will only put forth to reduce those impurities.*

As for recrystallization and what it involves, we can do no better than quote from the expert evidence of Prof Robert McClelland:

> *In its simplest form, the crystallization process consists of: (i) dissolving the impure substance in some suitable solvent at or near the boiling point; (ii) filtering the hot solution from particles of insoluble material and dust; (iii) allowing the hot solution to cool thus causing the dissolved substance to crystallize out, and (iv) separating the crystals from the supernatant solution (or mother-liquor). The resulting solid, after drying, is tested for purity (usually by melting point determination, but also by spectroscopic methods or by thin-layer chromatography), and if found impure is again recrystallized from fresh solvent. This process is repeated until the pure compound is obtained; this often means until the melting point is unchanged, but confirmation by the other methods specified above is desirable.*

According to Prof McClelland by 1980, solvents that could be employed for such recrystallization were well established. They included water, ethanol, acetone and ethyl acetate. Methods for determining the recrystallization solvent were also well established. The use of mixed solvents or solvent pairs was also a well-established practice.

As regards the preparative HPLC (which stands for high performance liquid chromatography), it is a tool for detecting compounds and could be used to separate out impurities from a compound. This was a method known before the priority date. This method was referred to in a paper published by the appellants in July 1980 in the Proceedings of National Academy of Science and the appellants` US patent application filed on 15 June 1979. Dr McClelland said that an example found in the appellants` Canadian patent, CP 380, also demonstrated the use of HPLC to separate compounds. He opined that as the appellants were able in CP 380 to separate the hydroxy acid from the Lovastatin, there was no doubt that the dimeric impurity was also well separated.

According to Dr Sailer, the technique HPLC was available in 1976 to detect the level of the dimer in the product.

Dr Barrett admitted that preparative HPLC could be used to separate impurities. Reliance is also placed by the respondents on the chromatogram produced by the appellants (pursuant to a specific discovery order) which showed that in March 1986 the appellants were capable of separating the dimer impurity from the hydroxy acid and other contaminents present by using HPLC.

At the end of the day, to determine whether there is an inventive step, what is claimed to be patentable must not be obvious. In the words of the trial judge `a person who is skilled in the art must not be able to apply known processes, forming part of the state of the art, to the manufacture of the claimed product.` He also cited the following rather helpful passage of Dillon LJ from **Genentech** [1989] RPC 203 at 276:

> *... in a case like the present, which does not involve a simple leap from the prior art to the invention ... but rather entails a journey with numerous steps taken in sequence, the court must ask itself by what routes it would have been possible to proceed to the goal from the starting point. Then the court must see what obstacles the skilled man would have faced on these routes, and must inquire how he could have overcome them, either in the way that the inventor himself overcame the obstacles on his chosen route or by circumventing or overcoming them in some other way, or by choosing another route from the outset, or by abandoning one route and choosing another. ... Having identified these various expedients, the court must finally ask whether they could have been overcome by pertinacity, sound technique or trial and error, with no more, or whether there would have been required a spark of imagination beyond the imagination properly attributable to the man skilled in the art.*

We also find the following observations of Whitford J, the first instance judge in ***Genentech*** , cited with approval by Dillon LJ in the Court of Appeal, highly illustrative:

> *to render an invention obvious it was not necessary that the material in question should have been the first choice of the notional research worker; it was enough that the material were `lying on the road` and there for the research worker to use.*

In this regard, we must also point out that the fact that a discovery is made does not mean there is an invention. The latter does not necessarily follow from the former. This distinction was brought out by Lindley LJ in ***Lane Fox*** (supra) at p 429 where he said:

> *An invention is not the same thing as a discovery. When Volta discovered the effect of an electric current from his battery on a frog`s leg he made a great discovery, but no patentable invention. Again, a man who discovers that a known machine can produce effects which no one before him knew could be produced by it, may make a great and useful discovery; but, if he does no more, his discovery is not a patentable invention: ... He has added nothing but knowledge to what previously existed. A patentee must do something more; he must make some addition, not only to knowledge, but to previously known inventions, and must so use his knowledge and ingenuity as to produce either a new and useful thing or result, or a new and useful method of producing an old thing or result.*

It should be borne in mind that the skilled addressee we are here concerned with is a process chemist, looking for ways to reduce impurities in lovastatin. What such a skilled addressee would do would have to depend on the problem he has to resolve. Will such a skilled addressee be able to achieve his ends, using the existing state of the art? In the light of the available techniques of purification, we would think so. The following concluding remark of Dillon LJ in ***Genentech*** is extremely germane:

> *We have a difficult art, in which the skill consists in a substantial degree of an ability to solve problems. It must, I consider, follow from this that the hypothetical skilled man must be credited with that particular ability in the appropriate degree.*

In the present case, the trial judge after reviewing the evidence found that numerous techniques, `myriad of processes`, were available to reduce the dimeric impurity present in the Lovastatin compound referred to in claims 16-21 and concluded that those claims were invalidated and should be revoked for lack of an inventive step. This is a finding of fact (see, eg ***Genentech***) and in the light of the evidence which were presented to court as we have outlined above, there is hardly any basis for us to say that the trial judge`s finding was plainly wrong, warranting the intervention of this appellate court. Indeed, we are inclined towards the view of the trial judge. There is evidence that supports the trial judge`s finding that using the standard techniques, such as recrystallization or activated carbon, would have been obvious to any person skilled in the art working to purify a compound like Lovastatin. We would agree that a person, skilled in the art, faced with impurities in a compound, would naturally use those techniques to reduce the impurities. In our opinion, what the appellants have achieved in the alleged patent is a discovery. It does not amount to an invention.

Miscellaneous point

We should mention in passing that in the appellants` Case they have made the point that claim 21 is irrelevant to the present action as it involves a different substance called simvastatin. However, in the respondents` Case they objected to this attempt by the appellants to exempt claim 21 from the proceedings at this stage when the statement of claim expressly put claim 21 in issue and the trial

proceeded on that basis. As there is no evidence before the court below that claim 21 is of a different substance and is not relevant, we think it is too late in the day for the appellants to take this course.

Judgment

In the premises, we hold that the respondents have not infringed the product claims because the patent in suit lacks an inventive step. The appeal is accordingly dismissed.

Turning to the question of costs, first we note that we do not think it is really helpful to the case for the respondents to raise the issue of `utility` and the question of purity per se. Second, we are not with the respondents on the issue of anticipation by prior disclosure. However, the respondents have succeeded on the inventive step point. But we appreciate that all these points are to some extent linked. There is furthermore one other relevant matter, ie the appellants have abandoned the point on the process claim. Taking all these into account, we think it fair that the respondents should only be entitled to 75% of the costs of this appeal. The security for costs, together with any accrued interest, shall be paid out to the respondents, or their solicitors, to account of their costs.

Outcome:

Appeal dismissed.