LUNDBECK AND CHEMICAL PRODUCT INVENTIONS

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The English courts in *Generics (UK) Ltd. v. H. Lundbeck A/S.*[2] arguably decided each of the two issues raised in the case incorrectly, but the end result demonstrates that two wrongs do make a right. At its core *Lundbeck* raises an old but perplexing conundrum. When should an inventor of a new chemical product receive full product patent protection for his invention?

The European patent[3] in *Lundbeck* claims escitalopram, the hugely successful SSRI[4] sold in the United States as Lexapro®. Escitalopram is one of the two enantiomers of the racemate citalopram. Lundbeck obtained its escitalopram patent over the closest prior art, citalopram itself.[5] Citalopram is sold in the United States as Celexa®. Mr. Justice Kitchen in his first instance opinion concluded that escitalopram's properties when compared to those of citalopram were truly unexpected. But then he said that was irrelevant on the issue of inventive step. He explained:

> 218. Professor Montgomery carried out a review of escitalopram for the Current Medicine Group, the second edition of which he re-wrote in 2005. He concluded that in vitro and in vivo studies had shown escitalopram to be a more potent SSRI than citalopram and that the (-) enantiomer is practically devoid of activity. This, of course, is described in the Patent. However, he also explained in his review and his evidence to me that a further surprising finding was that studies with some animal models had shown an earlier response to escitalopram compared to citalopram. Further, the role of the (-) enantiomer had been investigated in a series of preclinical studies, which had shown that that the (-) enantiomer reduces or delays the effect of the (+) enantiomer.
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> 219. Data supporting these conclusions came from experiments carried out on rats by Mork et al . . . . Surprisingly, when 2mg/kg escitalopram was compared to 4mg/kg citalopram, escitalopram elicited an increase in brain

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[2] [2007] EWHC 1040, rev'd in part [2008] EWCA Civ 311, affirmed [2009] UKHL 12.

[3] EP 0,347,066.

[4] Selective serotonin reuptake inhibitors (SSRIs) are a class of antidepressants that increase the extracellular level of the neurotransmitter serotonin by inhibiting its reuptake into the presynaptic cell, thereby increasing the level of serotonin available to bind to the postsynaptic receptor.

[5] Citalopram is sold in the United States as Celexa®.

serotonin levels that was about twice that with citalopram. Further, when escitalopram was administered together with twice or four times as much (-) citalopram, the (-) enantiomer significantly inhibited the (+) enantiomer induced increase in serotonin level in a dose-dependent manner. Professor Montgomery considered that these ratios of (+) to (-) enantiomers are clinically relevant because, in humans, the two enantiomers are metabolised at different rates, the (-) enantiomer being metabolised more slowly that the (+) enantiomer. The results showed, in his opinion, that escitalopram alone is more effective at increasing extra-cellular serotonin levels in the brain than an equivalent dose of citalopram, and that the (-) enantiomer counteracts the activity of the (+) enantiomer in vivo. Thus escitalopram is not only more potent than citalopram, but also more efficacious. I did not understand there to be any serious challenge to this analysis of the work by Mork, and I accept it.

220. Professor Montgomery also considered the binding mechanism of escitalopram. He noted that there were at least two binding sites for citalopram on the serotonin transporter: a primary high affinity binding site that mediates the inhibition of serotonin reuptake and a secondary low affinity allosteric site. He explained that work published in 2005 had shown that escitalopram increased the stabilisation of the binding to the serotonin transporter via the allosteric mechanism compared to other SSRIs and venlafaxine, and this went a long way to explaining the obvious clinical superiority of escitalopram as an antidepressant and anxiolytic. Once again, I accept this analysis of the binding action of escitalopram. I turn now to consider the clinical data said to show the superior efficacy of escitalopram.

He then analyzed clinical data regarding escitalopram which clearly demonstrated its unexpected efficacy. Nevertheless he explained that Lundbeck cannot rely on these unexpected benefits to prove nonobviousness because they are a bonus[6] or a "gratis effect"[7] and in addition the unexpected efficacy was not set forth in the specification:

231. As I have found, escitalopram does have unexpected benefits which could not have been predicted from a simple consideration that it was likely that one enantiomer was primarily responsible for the action of citalopram.

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[6] The leading English case discussing the idea that the so-called bonus is not credited to the inventor, but instead can be claimed by the public is Hallen Co. v Brabantia (U.K.) Ltd., [1991] RPC 195 (Ct. App.).

[7] See n8, infra.

232. But there is one other material matter I must take into consideration. There is no suggestion of such surprising benefits in the Patent itself, as Professor Montgomery accepted. It reports that the inventors have found that the (-) enantiomer is essentially ineffective and that the (+) enantiomer is about twice as effective as the racemate - in fact it needs slightly more than half a unit dose of the (+) racemate to produce the same effect as a unit dose of the racemate. This is what the skilled person would expect of a racemate where the activity lies in one of the two enantiomers. The data in the Patent does not indicate the greater efficacy found in practice.

233. There is no doubt that a surprising technical benefit can be regarded as an indication of inventive step. But whether it does so or not depends upon all the circumstances. For example, if it is found that the claimed invention is obvious for one purpose then it is not saved because it is found to have added benefits: Hallen v Brabantia . . . at 216.

234. Likewise, I do not believe it is permissible to take into account surprising technical benefits which are not described or foreshadowed in the specification. In Richardson-Vicks Inc.'s Patent . . ., the alleged invention related to mixtures of a non narcotic analgesic with one or more of an antihistamine, a decongestant, an expectorant and a cough suppressant, to be sold for the treatment of coughs and flu. The patentee argued that the combination had an unexpected advantage resulting from synergy between its components. Jacob J said at 581:

> "Formally I think the experiments were irrelevant. Curiously Mr Thorley, for the purpose of his argument before me, accepted this. Whether or not there was synergy demonstrated by experiments conducted after the date of the patent cannot help show obviousness or non-obviousness. Nor can the amended claim be better if only the components of the amended claim (as opposed to the unamended claim) can be shown to demonstrate synergy. The patent does not draw any such distinction and it would be quite wrong for later acquired knowledge to be used to justify the amended claim."

235. In Glaxo Group Ltd's Patent. . ., Pumfrey J took much the same line. The patent related to an inhaler that administered simultaneous doses of two drugs, salmeterol and fluticasone propionate. The specification taught that they should be administered together but gave no data to support any assertion that they were particularly compatible or complementary in their activity. The patentee sought to rely upon evidence to show synergy between the elements of the combination but ultimately abandoned any attempt to rely upon synergy per se. The judge explained at [113]:

> "It is sometimes thought that a patent may be saved from a finding of obviousness if a combination otherwise obvious has some unexpected advantage, and, in particular, an advantage caused by an unpredictable co-operation between the elements of the combination. I do not consider that such an approach is in general justified. There is a limited class of cases in which the patentee has identified an advantageous feature possessed by some members only of a class otherwise old or obvious, has described the advantageous effect in his specification and has limited his claim to the members of the class possessing this advantageous feature. Such a claim may be justified on the basis of what is called selection. Unexpected bonus effects not described in the specification cannot form the basis for a valid claim of this kind. "

236. After referring to the passage from Richardson-Vicks cited above, he continued at [114]:

> "If a synergistic effect is to be relied on, it must be possessed by everything covered by the claim, and it must be described in the specification. No effect is described in the present specification that is not the natural prediction from the properties of the two components of the combination."

237. Both of these cases were concerned with synergy. But it seems to me that the logic behind them is not limited to such cases. A patentee cannot seek to bolster the inventive nature of his monopoly by relying on a discovery which he had not made at the time of the patent. That is the position here. At the date of the Patent, Lundbeck had not found that escitalopram was more efficacious or was effective in treating more patients than citalopram. Those discoveries were not made until some time later. They are nowhere hinted at in the specification and could not have been predicted from what is described. In these circumstances I do not believe that it is legitimate for Lundbeck to rely upon them in support of the alleged invention.

The implication of Mr. Justice Kitchen's reasoning is that the invention was not made as of the filing date because separating the two enantiomers of citalopram and testing them to show which was the active one, but not as yet determining that the inactive enantiomer was actually inhibiting the efficacy of citalopram, was all for naught. The inventors had filed too early. They should have waiting until they learned of the actual role of the inactive enantiomer. There was no reason to believe before they did their work that one of the enantiomers would be a better SSRI than numerous other possible modifications of citalopram. It turned out that escitalopram was remarkably

good, but to deny Lundbeck a patent on the basis that it really didn't appreciate at the time just how good escitalopram really is, is simply unfair and bad public policy.

In two recent EPO Board of Appeal decisions,[8] the respective boards also disregarded certain properties of the claimed compounds because these properties are mere "gratis effects." For example in T 0215/01 which involved a specific new use of methylene blue, the Board explained:

> Since, for the above, reasons, the skilled person would automatically first have envisaged the use of the methylene blue without the exercise of inventive ingenuity, any additional advantage (e.g. high activity, different mechanism of action), even if it was unexpected, could only be considered as a gratis effect which would inevitably have resulted from the skilled person's non-inventive activity.[9]

The obvious problem with this way of thinking is that the problem solution approach to the question of inventive step depends on how the problem is defined. If the problem includes the unexpected features including the "gratis effect" such as saying that the problem with respect to the escitalopram patent is finding a compound that is similar to citalopram, but having the features that were ultimately found to be unexpected, then going from citalopram to escitalopram involves an inventive step. Of course if the problem is simply to find the best enantiomer of the two enantiomers of citalopram, then the unexpected features are a bonus or "gratis effect" and hence going from one to the other did not involve an inventive step. In short, the problem solution approach adds nothing of value to the policy question of when a product claim involves an inventive step. The better approach and the one adopted in the United States is to credit the inventor with all of the properties of the product which he creates.[10] An inventor

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[8] T 1212/01 and T 0215/01

[9] ¶ 4.3.5.

[10] Application of Papesch, 315 F.2d 381 (C.C.P.A. 1963; Commission of Patents v. Deutsche Gold-Und Silber-Scheideanstalt Vormals Roessler, 397 F.2d 656 (D.C. Cir. 1968).

should be given credit for what he in fact contributes to the art whether it is due to good luck or innate inventive genius or just sheer hard work. Society should not slice and dice the contribution as is done under the bonus or "gratis effect" doctrine.

The appropriate battle regarding product protection for new compounds is whether the inventor of a new chemical product along with a use for that product should receive a use patent or a product patent. There are arguments for both points of view each based on the proposition that an inventor should receive protection commensurate with what he contributes to society. The leading case in the United States arguing for use protection only is *Carter-Wallace, Inv. v. Davis-edwards Pharmacal Corp.*,[11] but its arguments have been generally rejected both in the United States and elsewhere on the theory that the inventor has both brought forth a new chemical product and discovered a nonobvious use for it. Thus this approach is consistent with the general notion that an inventor is entitled to a claim covering what he or she contributed. Hence the inventors in *Lundbeck* contributed escitalopram and its unexpected properties. That should have been sufficient for Mr. Justice Kitchen to have awarded Lundbeck product patent protection..

Ironically Mr. Justice Kitchen, after deciding that the properties of escitalopram would not support patentability, pivoted to the question of whether the disclosed enantiomer separation method was itself nonobvious and if so whether this disclosure was sufficient to support a pure product claim. He decided that the answer was that it was not sufficient since such a claim would cover a newly discovered method for separating the enantiomers that was not literally covered by the claims to the disclosed nonobvious method or an equivalent thereof . He supported his decision by referencing the landmark case

[11] 341 F. Supp. 1303 (E.D.N.Y. 1972).

of *Biogen Inc. v. Medeva plc*,[12] as its product claims were essentially treated as process claims and the inventors were not given control over other future methods of making the claimed antigens. Mr Justice Kitchen explained his reading of *Biogen* with reference to the priority disclosure known as Biogen I:

> 259. Lord Hoffmann then turned to consider whether Biogen I contained an enabling disclosure which supported the claims of the patent. He accepted that the teaching of Biogen I enabled the skilled man to produce both HBcAg and HBsAg in any cells and, in that sense, to produce products across the scope of the claim. However that was not the end of the matter. At pages 50-51 he said:
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> > But the fact that the skilled man following the teaching of Biogen 1 would have been able to make HBcAg and HBsAg in bacterial cells, or indeed in any cells, does not conclude the matter. I think that in concentrating upon the question of whether Professor Murray's invention could, so to speak, deliver the goods across the full width of the patent or priority document, the courts and the E.P.O. allowed their attention to be diverted from what seems to me in this particular case the critical issue. It is not whether the claimed invention could deliver the goods, but whether the claims cover other ways in which they might be delivered: ways which owe nothing to the teaching of the patent or any principle which it disclosed.
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> > It will be remembered that in Genentech I/Polypeptide expression the Technical Board spoke of the need for the patent to give protection against other ways of achieving the same effect "in a manner which could not have been envisaged without the invention". This shows that there is more than one way in which the breadth of a claim may exceed the technical contribution to the art embodied in the invention. The patent may claim results which it does not enable, such as making a wide class of products when it enables only one of those products and discloses no principle which would enable others to be made. Or it may claim every way of achieving a result when it enables only one way and it is possible to envisage other ways of achieving that result which make no use of the invention.
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> > One example of an excessive claim of the latter kind is the famous case of O'Reilly v. Morse (1854) 56 U.S. (15 How.) 62 in the Supreme Court of the United States. Samuel Morse was the first

[12] [1997] RPC 1 (H.L.).

person to discover a practical method of electric telegraphy and took out a patent in which he claimed any use of electricity for "making or printing intelligible characters, signs, or letter, at any distances". The Supreme Court rejected the claim as too broad. Professor Chisum, in his book on Patents (vol. 1, § 1.03[2] summarises the decision as follows:

> "Before Morse's invention, the scientific community saw the possibility of achieving communication by the .galvanic' current but did not know any means of achieving that result. Morse discovered one means and attempted to claim all others."

A similar English case is British United Shoe Machinery Co. Ltd. v. Simon Collier Ltd. (1908) 26 R.P.C. 21. The patentee invented a piece of machinery for automatically trimming the soles of boots and shoes by means of a cam. One of the claims was in general terms for automatic means of trimming soles. Parker J. said, at pages 49-50:

> "[T]he problem was simply how to do automatically what could already be done by the skill of the workman. On the other hand, the principle which the inventor applies for the solution of the problem is the capacity of a cam to vary the relative positions of two parts of a machine while the machine is running. Assuming this principle to be new, it might be possible for the inventor, having shown one method of applying it to the solution of the problem, to protect himself during the life of his patent from any other method of applying it for the same purpose, but I do not think that the novelty of the principle applied would enable him to make a valid claim for all means of solving the problem whether the same or a different principle were applied to its solution."

260. Applying these principles to the facts of the case before him, Lord Hoffmann concluded that the technical contribution made by Professor Murray did not justify a claim to a monopoly of any recombinant method of making the antigens. Its excessive breadth was not due to an inability to produce all the claimed results, but due to the fact that the same results could be achieved by different means. Professor Murray had established no new principle which all his successors had to follow if they were to produce the same results. It was not enough that Professor Murray had showed by his invention that the expression of Dane particle DNA in a host cell could be done. As Lord Hoffmann explained at page 52:

> "…care was needed not to stifle further research and healthy competition by allowing the first person who has found a way of achieving an obviously desirable goal to monopolise every other way of doing so. "

261. Finally, Lord Hoffmann confirmed that the reasoning by which he had come to the conclusion that the patent was not entitled to the claimed priority also led to the conclusion it was insufficient.

262. In this case Lundbeck submitted that the technical contribution of the Patent was the discovery and realisation of a new and non obvious compound, the (+) enantiomer. It was not an obvious goal. No one had produced or tested it before the priority date. Further, Lundbeck had shown a way of making it and so the Patent was sufficient.

263. I accept that if a patentee describes a new and non obvious compound which has a beneficial effect and describes a way by which it can be made then he is entitled to a patent for the compound. This is made clear in the passage from the speech of Lord Hoffmann which I have cited in paragraph [260] above. In such a case the technical contribution lies in the provision of the new and useful compound. Others might find different ways of producing it. But this does not render the original patent insufficient because in each case they are making use of the technical contribution – the knowledge they are making the new and useful compound.

264. In my judgment this is not such a case. For the reasons I have set out at length earlier in this judgment I am satisfied that medicinal chemists working in the field of SSRIs at the priority date considered it obviously desirable to separate out and test the enantiomers of active racemates. True it is that in the case of citalopram no one knew the activity would lie in the (+) enantiomer. However it was entirely obvious that the activity might lie primarily in one enantiomer rather than the other. Further, once the enantiomers had been separated the tests which the inventors carried out to determine where the activity lay were routine and straightforward, as were the steps necessary to formulate the (+) enantiomer into a pharmaceutical composition. The inventive step taken by the inventors of the Patent was not deciding to separate the enantiomers of citalopram but finding a way it could be done. The technical contribution they made was the discovery that the diol intermediate could be resolved and then the enantiomers of the diol converted into the enantiomers of citalopram whilst preserving their stereochemistry.

265. Claims 1 and 3 of the Patent cover all ways of making the (+) enantiomer of citalopram. For example, they cover resolving citalopram on a preparative chiral HPLC column. Does this method of resolution owe anything to the teaching of the Patent or any principle it discloses? In my judgment it does not. By June 1988 the preparation of the individual enantiomers of citalopram was an obviously desirably goal and their testing was trivial. There is no teaching in the Patent as to how that goal is to be achieved other than by the use of the diol intermediate. Just as in Biogen, it not enough to say that the inventors showed that resolution could be done and that they found the activity lay in the (+) enantiomer. The first person to find a way of achieving an obviously desirable goal is not permitted to

> monopolise every other way of doing so. Claims 1 and 3 are too broad. They extend beyond any technical contribution made by Lundbeck.

The discussion above is fascinating because it is true that the function of both enablement and obviousness is to align the contribution of the inventor with the scope of the monopoly grant. Enablement does this by insuring that everything except dependent inventions covered by any valid claim is given to the public without undue experimentation and obviousness performs its function by insuring that everything covered by any valid claim except dependent inventions are not obvious. In short everything but dependent inventions must be put in the hands of the public by the disclosure (enabled) and everything covered by the claims must be nonobvious. Lord Hoffmann' s speech in *Biogen* was based on this proposition for the patented genes for the antigens were discovered by a process that was primitive, a process that would no doubt be superceded in a few months as it truly was by methods of probing gene libraries. Thus Lord Hoffmann reasoned that the inventors were entitled only to antigens made from genes found by the primitive process disclosed in Biogen I even though the claims were drafted in the form of product claims. To put this in raw terms well-known to lawyers in law firms, inventors are only to eat what they kill.

In *Lundbeck*, however, the question was not the scope of the claim, but whether an obvious product is patentable if there is no known obvious method of making it. The product must be consider obvious because the special properties beyond those expected of one enantiomer of a racemate were not considered by the court. Giving the inventor of an obvious product a patent on that product because of the invention of a nonobvious process for making it arguably overcompensates the inventor as it puts the inventor in a position to control all methods of making the obvious product as well as provide control over all discoveries of new uses of the product. Why this apparent overcompensation of the inventor? Why this failure to align the invention with the reward? Why this ability to eat more than you killed?

In the famous case of *In re Hoeksema*,[13] the Court of Customs and Patents Appeals did not directly answer any of these questions. Neither did Lord Hoffmann[14] when *Lundbeck* reached the Court of Appeal for all Lord Hoffmann did in his opinion is correctly point out that the claim in *Lundbeck* was enabled as it surely was and that the claims in *Biogen* were really a special form of method claims albeit seemingly product claims. As for granting product protection for an obvious product, Lord Hoffmann simply said that was the law applicable in the European Patent Office (EPO) and the UK courts should follow the lead of the EPO. Lord Justice Jacob, another leading patent jurist, went further and tried to rationalize the result. He explained:

> 53. Where then, lay the Judge's error? He reasoned thus: that the (+) enantiomer existed was known. So all that Lundbeck "invented" - contributed to the art - was a particular way of making it. So its patent claim should be correspondingly limited. Were it otherwise, Lundbeck would effectively get a monopoly to any way of making the (+) enantiomer – ways which it had not invented. Hence the claim was insufficient.
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> 54. But any product claim is apt to give the patentee "more than he has invented" – and in two ways. Firstly such a claim will have the effect of covering all ways of making the product including ways which may be inventive and quite different from the patentee's route. Secondly it will give him a monopoly over all uses of the patented compound, including uses he has never thought of.
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> 55. I elaborate on the second point a little. A patent can only be granted for a novel substance if the patentee specifies a use for it (absent this he has simply not made an invention at all – has added nothing to human knowledge). But once he has specified a use, his claim to the substance will cover any use. For instance he may invent a new glue, specified in his claim by its chemical composition. If that glue turns out to be useful for some entirely different purpose, e.g. as a plasticiser, he has a monopoly over that too – more than he "invented".
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> 56. It works the other way round too. If a substance is old, it may not be repatented as such just because the later inventor has found an entirely different use. An old but good example of this is *Shell v Esso* [1960] RPC 35 where the prior art disclosed a fuel with an additive for preventing corrosion of fuel tanks and the patentee wanted a claim to a fuel with the same additive for the quite

[13] 399 F.2d 269 (CCPA 1968).

[14] Sitting in the Court of Appeal.

different purpose of increasing octane rating and prevention of fouling of plugs and valves. The patentee had to disclaim those parts of his claimed range with overlapped with the prior art range. (It now may be possible for a patentee to do somewhat better by the use of the kind of claim approved by the Enlarged Board in *MOBIL/Friction reducing additive GO2/88*, namely "the use of that compound in a composition for a particular purpose").

57. The fact that compound claims may give a patentee "more than he deserves" has not in practice proved to be much of a problem. Their certainty and pragmatic value has proved itself over the years. What matters for present purposes is that the concept "that the patentee should not have more than he deserves" does not form part of the statutory test for sufficiency.

58. The other consideration which moved the judge was this: that the claim was to a desired compound. He thought the position would be different if the technical contribution lay in "the provision of the new and useful compound." Here, that the compound would be useful was already known, so the monopoly should not extend to it.

59. It is of course the case that, as the Technical Board of Appeal said in *Exxon/ Fuel Oils* T409/91 at 3.3:

> "The extent of the patent monopoly, as defined by the claims, should correspond to the *technical contribution* to the art in order for it to be supported or justified."
> In the context of substance claims the technical contribution includes provision of the substance itself – one that could not be provided before. Merely because it was wanted before does not diminish the technical contribution.

60. Some careful thinking is called for in considering claims to desirable ends. There are different sorts of these. I quite agree that a patentee may not normally frame his claim simply by reference to known desirable properties of a product – what is sometimes called a "free beer" claim. The Guidelines for Examination at the EPO put it this way:

> "4.1 The area defined by the claims must be as precise as the invention allows. As a general rule, claims which attempt to define the invention by a result to be achieved should not be allowed, in particular if they only amount to claiming the underlying technical problem."
> and:
> "4.10 Result to be achieved
> The area defined by the claims must be as precise as the invention allows. As a general rule, claims which attempt to define the invention by a result to be achieved should not be allowed, in particular if they only amount to claiming the underlying technical problem. However, they may be allowed if the invention

> either can only be defined in such terms or cannot otherwise be defined more precisely without unduly restricting the scope of the claims and if the result is one which can be directly and positively verified by tests or procedures adequately specified in the description or known to the person skilled in the art and which do not require undue experimentation (see T 68/85, OJ 6/1987, 228)."
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> 61. So, for example, if a man finds a particular way of making a new substance which is 10 times harder than diamond, he cannot just claim "a substance which is 10 times harder than diamond." He can claim his particular method and he can claim the actual new substance produced by his method, either by specifying its composition and structure or, if that cannot be done, by reference to the method (see *Kirin-Amgen* at [90-91]) but no more. The reason he cannot claim more is that he has not enabled more – he has claimed the entire class of products which have the known desirable properties yet he has only enabled one member of that class. Such a case is to be contrasted with the present where the desirable end is indeed fully enabled – that which makes it desirable forms no part of the claim limitation.
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> 62. Those examples form two extremes – there may be cases in between where the invention may lie in appreciating that a particular combination of desirable properties is of special value. The validity of that sort of claim will be particularly sensitive to the context of the teaching of the patent and the prior art.
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> 63. Finally I should say a word about *Biogen.* I can well understand that certain passages, taken out of context, can be read as supporting the Judge's decision. But none of them was concerned with a case like this: a novel, non-obvious and enabled product claim. In the end one comes back to the short answer with which I started this topic. Founded as it is on the plain words of the statute I do not see how it can be refuted.

The speeches by the law lords also failed to answer this fundamental question. Hence while all of the appellate judges departed from the principle that aligns the reward with the invention, they apparently did so because of the position of the EPO, an approach which is in line with *Hoeksema*, a case which has been followed in the United States in important cases such as *Amgen, Inc. v. Chugai Pharmaceutical Co*.[15] and *Scripps Clinic & Research Foundation v. Genentech, Inc*.[16]

[15] 927 F.2d 1200 (Fed. Cir. 1991).

[16] 927 F.2d 1565 (Fed. Cir. 1991).

In *Hoeksema* the key issue was the patentability of N-psicofuranoside compounds where the prior art disclosed a compound having an amino group at the 6-position of the purine ring system. The claimed compounds defined over this compound by having the following groups at the 6-position of the purine ring system, hydrogen, the group -XR where XR includes many groups including substituted amines, but of course excluding the amino group itself. The CCPA considered that the claims defined obvious compounds, but the method of positioning such groups at the 6-position of the purine ring system was very difficult once the amino group was excluded. Nevertheless the CCPA held the claims in Hoeksema' s application to be patentable explaining:

> (1) Appellant will admit his compounds are obvious and unpatentable if an obvious process is available to make them. Does it follow then that appellant's compounds are unobvious and patentable if an obvious process is not available to make them?
> Within this context, appellant simplifies that question to: Is process obviousness relevant in deciding compound obviousness?
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> We think appellant really means to say that the question is whether a claimed compound may be said to be legally obvious when no process for making that compound is shown in the prior art relied upon to establish legal obviousness under *section 103*.
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> The solicitor responds to the latter characterization of the question in the affirmative, pointing out that the first question bears on the principle implicit in *In re Brown, supra*, that claimed compounds not distinguished in their properties over closely related prior art compounds are unpatentable thereover where the claimed compounds would be "in possession of the public" in that a process for preparing them would be obvious to those of ordinary skill in the art.
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> In addition, the solicitor now refers to our prior opinion in which we noted that the facts in this case are closely analogous to those of *In re Riden,* . . ., where we stated that the fact that the method of making the claimed compound is relevant, ...
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> A recurring problem of analysis which confronted us as we prepared our previous opinion, and which still confronts us after the rehearing, has its genesis in a proper understanding of the issue as framed by appellant. In effect, appellant agrees that since the claimed product is a homolog of a known compound, it would be prima facie "obvious" under *35 USC 103*. But this agreement is

conditioned on the proviso that there is in the prior art an "obvious" process by which to make that compound.
In the context of *section 103*, we are not permitted to fragment a claimed invention in applying that section. The clear mandate of the statute which governs our analysis requires that we consider the invention as a whole in making the determination.

Thus, as we apply the statute to the present invention, we must ask first, what is the invention as a whole? Necessarily, by elementary patent law principle, it is the claimed compound, but, so considered, unless there is some known or obvious way to make the compound, the invention is nothing more than a mental concept expressed in chemical terms and formulae on a paper.

We are certain, however, that the invention as a whole is the claimed compound and a way to produce it, wherefore appellant's argument has substance. There has been no showing by the Patent Office in this record that the claimed compound can exist because there is no showing of a known or obvious way to manufacture it; hence, it seems to us that the "invention as a whole," which *section 103* demands that we consider, is not obvious from the prior art of record.

While there are valid reasons based in public policy as to why this defect in the prior art precludes a finding of obviousness under *section 103*, *In re Brown*, *supra*, its immediate significance in the present inquiry is that it poses yet another difference between the claimed invention and the prior art which must be considered in the context of *section 103*. So considered, we think the differences between appellant's invention as a whole and the prior art are such that the claimed invention would not be obvious within the contemplation of *35 USC 103*.

While *35 USC 102* is not directly involved in the issue on review, the conditions for patentability, novelty and loss of right to patent, there stated, may have relevance as to the disclosure which must be found in the prior art to find obviousness of an invention under *section 103*. In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention "not novel" or "anticipated" within *section 102*, the stated test is whether a reference contains an "enabling disclosure," in the present context, a process by which the claimed compound could be made. In *In re Le Grice, . . .*, we observed that the resolution of this issue required us to determine whether, as a matter of law, a reference without such a disclosure constituted a statutory time bar to an applicant's right to a patent. There, the issue was founded on *35 USC 102(b)*, not 103, but our conclusions have a certain pertinence here. We concluded, . . .:

> We think it is sound law, consistent with the public policy underlying our patent law, that before any publication can amount to a statutory bar to the grant of a patent, its disclosure must be such that a skilled artisan could take its teachings in combination with his own knowledge of the particular art and be in possession of the invention.

* * *

> Thus, upon careful reconsideration it is our view that if the prior art of record fails to disclose or render obvious a method for making a claimed compound, at the time the invention was made, it may not be legally concluded that the compound itself is in the possession of the public. In this context, we say that the absence of a known or obvious process for making the claimed compounds overcomes a presumption that the compounds are obvious, based on close relationships between their structures and those of prior art compounds.[17]

It is also noteworthy that in the corresponding case to *Lundbeck* in the United States, *Forest Lab. Holdings, Inc. v. Ivax Pharma., Inc*.[18] the Federal Circuit upheld the following arguments of Forest Laboratories showing that the Federal Circuit relied on both the unexpected properties and the nonobvious method to support its decision that escitalopram is patentable over citalopram:

> In response, Forest argues that any prima facie obviousness based on racemic citalopram was rebutted by the evidence demonstrating the difficulty of separating the enantiomers and the unexpected properties of (+)-citalopram. Forest argues that it was unexpected that all of the therapeutic benefit of citalopram would reside in the (+)-enantiomer, resulting in escitalopram having twice the potency of racemic citalopram. Forest also argues that the district court was entitled to credit evidence that a person of ordinary skill in the art would not easily have turned to the diol intermediate to attempt resolution of racemic citalopram both because of the uncertainty involved and because Wilen and Jacobus describe compounds less complex than those necessary here to resolve the diol intermediate and then convert the (-)-diol enantiomer to escitalopram.[19]

Turning now to what is perhaps the most important and soundly based application of the *Hoeksema Lundbeck* approach, gene inventions covering naturally occurring proteins where at least everywhere but in the United States the patentability of such a gene is judged by the obviousness or nooobviousness of the method for isolating it. In the United States under *In re Deuel*[20] all such gene inventions are considered

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[17] 399 F.2d at 272-74.

[18] 501 F.3d 1263 (Fed. Cir. 2007).

[19] 501 F.3d at 1269.

[20] *51 F.3d 1552 (Fed. Cir. 1995).*

nonobvious so it is not necessary to look at the obviousness of the method of its isolation. However, *Deuel* is being challenged under *KSR v. Teleflex*[21] in the appeal to the Federal Circuit of *Ex parte Kubin*.[22] *Kubin* took the approach that the law applied in the rest of the world should also apply in the United States with respect to gene patents. I submit that the patent system has no choice but to give product protection to gene patents where the invention is a nonobvious method of isolating the gene as that method will never be used again once the gene is isolated so a method claim to what is essentially a method invention would be worthless. The law then has the choice of overcompensating the inventor under the *Hoeksema Lundbeck* approach or giving the inventor a claim on what he actually invented, which in the special case of genes covering natural products is valueless. Given this choice, overcompensation makes good sense. The same may be true for a nonobvious method of purification where the purification leads to the discovery of the chemical formula which in turn leads to a synthetic method for making the purified product. However, in the usual situation where the method will be practiced over and over again why should it matter that one day inventor A files a patent application with a disclosure of an obvious product X and a process to make X that is not obvious. However, a few days earlier a close friend of B who works as an independent inventor told B that he was just about to publish an article describing a new discovery of his and that he was keeping the discovery secret until publication. B immediately realizes that based on this discovery he could quickly develop an obvious process for making X and he promptly did just that. B then filed a patent application covering X believing that X is not obvious as B is not familiar with all of the available prior art. Setting aside issues of priority, does it make sense that A would be able to get a patent on X, but B would not? *Hoeksema* and *Lundbeck* say that the answer is "yes."

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[21] 127 S.Ct. 1721 (2007).

[22] 83 U.S.P.Q.2d 1410 (BPAI 2007).