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Credible Utility in Patent Law

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CREDIBLE UTILITY IN PATENT LAW

The law relating to the patentability of products and methods of their use is one of the most vexing in the field of patent law. It was not always so. Take for example patents on novel machines. New machines are the work of inventors building on the inventions of others. Normally it is fairly easy to see if the machine does what it was designed to do and there is little question of the utility or industrial applicability of newly invented machinery. While mechanical inventions make use of modern science and mathematics, in their very essence mechanical inventions are not the product of the scientific revolution. Further, many inventions that are derived from the scientific revolution in fields such as for example electronics and computer related inventions fit the template developed for mechanical inventions. But does this template fit products found in nature in an impure state and subsequently isolated and purified by inventors? In addition, the same question can be asked about products made by chemical processes whose use or industrial applicability is not readily apparent.

If we focus for a moment on products made by chemical processes which have no known use, such products can only be viewed as nonobvious if the process for making them is itself nonobvious. This fact pattern presents an important patent law question, does the product need to have a use or industrial applicability in order to issue a patent to its inventor beyond simply providing the product for experimentation designed to find uses for it? The general answer is yes. However, that answer will undoubtedly lead an inventor who has brought forth a product which has no known credible utility or industrial applicability to add some guesses to her patent application in the hopes that if she guesses correctly she will

obtain a valuable patent. If one of the guesses proves correct should this be treated in essence as a constructive reduction to practice sufficient to justify the grant of a valid patent?

This paper suggests that the proper answer should be no because a sound patent system should not encourage guessing where there is no sound scientific basis for the guess. My analysis of how such guesses are treated in patent law starts with one of the most remarkable patent cases of the last decade, *Conor Metasystems v. Angiotech*.¹ It will end with a possible explanation of why the Federal Circuit may have created the new doctrine of description as applied to originally filed claims.

CONOR METASYSTEMS v. ANGIOTECH

Conor Metasystems involved the overturning of the decisions of two leading patent jurists, Lord Justice Jacob² and the late Sir Nicholas Pumfrey³ by the House of Lords. Both jurists held that Angiotech's taxol coated stent patent was invalid. It is hard not to conclude from the facts set out in both opinions that the Angiotech inventors had made at most a trivial advance over the prior art, an advance unworthy of a patent. Unfortunately both jurists used obviousness to hold the patent invalid. I shall argue in this paper that the disclosure of the claimed invention was speculative and thus Angiotech's patent should have been held invalid based on the speculative nature of the disclosure, a defense not raised by Conor Metasystems.

Claim 12 of EP 706,376 ('376), Angiotech's patent, written in independent form without its redundant language reads

12. A stent for expanding the lumen of a blood vessel comprising a generally tubular structure coated with taxol, or an analogue or derivative thereof, for treating or preventing recurrent stenosis.

¹ [2008] UKHL 49.

² [2007]EWCA Civ 5.

³ [2006]EWHC 260 (Pat).

In short, the claim is for a taxol coated stent used with angioplasties for treating or preventing recurrent stenosis (restenosis), a phenomenon often observed in clogged vessels opened by angioplasty. The patent suggests that taxol is a good drug to use for coating the stent to diminish restenosis. However, the idea of using a drug that attacks cell growth to coat a stent was old in the art. Medtronic's WO 91/12779 patent application published two years before Angiotech's filing date discusses various classes of drugs that may be used to coat the stent. Taxol was not specifically mentioned, but it was a member of a specific class of drugs discussed in the Medtronic application.

The Angiotech '376 specification is a lengthy document focusing on the testing of various compounds for their ability to block the formation of blood vessels, anti-angiogenesis compounds. The disclosed tests showed that taxol was a powerful inhibitor of angiogenesis. Based on these angiogenesis tests Angiotech's inventors proposed the use of taxol coated stents for use in the palliative treatment of advanced cancer since the cancer itself often grows in a way that closes the lumen created by the stent. Given the scientific understanding at the time regarding angiogenesis and cancer, the use of an anti-angiogenic compound such as taxol on a stent placed in an area of a growing cancer to keep a body passage open for palliative treatment of that cancer made scientific sense. The theory of using drugs that block the development of new blood vessels as a method of treating cancers was not mentioned in Angiotech's patent although it dates back at least to the 1970s owing to the pioneering work of the late Dr. Judah Folkman.

But the lengthy Angiotech patent specification, however, almost as a throw away, includes the following paragraph:

[0077] Within another embodiment of the disclosure, methods are provided for eliminating vascular obstructions, comprising inserting a vascular stent into a blood

vessel, the stent having a generally tubular structure, the surface of the structure being coated with an anti-angiogenic composition as described above, such that the vascular obstruction is eliminated. Briefly, stents may be placed in a wide array of blood vessels, both arteries and veins, to prevent recurrent stenosis at the site of failed angioplasties, to treat narrowings that would likely fail if treated with angioplasty, and to treat post surgical narrowings (eg dialysis graft stenosis). Representative examples of suitable sites include the iliac, renal and coronary arteries, the superior vena cava, and in dialysis grafts.

Well there you have it, coat stents with an anti-angiogenic composition such as taxol and you can prevent restenosis, an overgrowth of normal cells caused by an attempt by the body to heal the artery after an angioplasty or stent placement. Obviously such an overgrowth can once more narrow the artery. There is no teaching whatsoever in the specification showing scientifically that anti-angiogenic compositions are the key to preventing this restenosis process. Indeed, there isn't today any reason to believe that to be true as Lord Hoffmann conceded as much in his speech, but what is true is the speculation regarding taxol has proved to be true as applied to angioplasties. It is not surprising then to learn that the commercial success of taxol coated stents owes nothing to the teachings of the Angiotech patent. The useful patent covering taxol coated stents stems from work at NIH by James L. Kinsella and Steven J. Sollott, U.S. Patent No. 5,616,608 and its corresponding European patent EP 711,158. Their work predated the filing date of Angiotech's patent, but their patents had a convention filing date of a few days after Angiotech's convention filing date, July 19, 1993 and July 29, 1993, respectively. Nevertheless, if one accepts that Angiotech's application clearly stated that it believed that taxol was an excellent drug for use with a stent for angioplasties and that speculation has proven to be substantially true, then the conclusion of the House of Lords that claim 12 was not obvious was sound as there was no particularly teaching in the prior art that would single out low dosages of taxol for the prevention of

restenosis as a clearly superior drug for this specific purpose. Moreover, from the point of view of enablement, the specification most certainly taught one skilled in the art how to make a taxol coated stent. Of course had taxol not worked in this environment which was surely likely as of the filing date, the claim would not have been valid.

Since the issue of industrial applicability was not raised in *Angiotech* on the theory that there was no scientific reason to believe that restenosis had anything to do with angiogenesis, the House of Lords did not have to deal with the speculative nature of the specification that supported claim 12. However, Sir Nicholas Pumfrey suggested that had it been raised he would have found the requirement of industrial applicability satisfied for he commented in the course of his opinion that “It is a fundamental principle that the disclosure of a specification to the skilled man at the relevant date is not to be assessed by reference to the work that the patentee had in fact done towards arriving at the invention claimed in the claims. It is entirely legitimate for a patentee to write a complete specification, experiments and all, without leaving his armchair, but he runs the risk of a finding of insufficiency if he gets anything wrong.” Given his belief in the legal soundness of speculative disclosures that prove to be true, it is not surprising that speculation was not raised before him as a defense. However, in *Human Genome Sciences v. Eli Lilly*⁴ there is at least a suggestion that Lord Justice Jacob does not agree with Sir Nicholas Pumfrey.

HUMAN GENOME SCIENCES

Early in 2010 Lord Justice Jacob in *Human Genome Sciences* discussed speculation in patent specifications. The main issue in the litigation involving EP 939,804 (‘804) was whether the industrial applicability requirement was met by the specification supporting

⁴[2010] EWCA Civ 33.

claims covering a newly discovered gene for a protein identified as neutrokin- α (now named TNF SF13b), a vector containing this gene and most importantly a claim to antibodies to neutrokin- α . The stimulus for the litigation was claim 13 which apparently covers the antibodies disclosed in Lilly's US patent No. 7,317,089. Claim 13 reads:

An isolated antibody or portion thereof that binds specifically to (g) the full length Neutrokin- α polypeptide (amino acid sequence of residues 1 to 285 of SEQ ID NO: 2); or (h) the extracellular domain of the Neutrokin- α polypeptide (amino acid sequence of residues 73 to 285 of SEQ ID NO: 2).

The '804 specification taught the role of neutrokin- α with reference to the group of proteins that belonged to the TNF family by using a computer analysis rather than by experimental data. The basic question for decision was whether its computer analysis was speculative or alternatively was enough to satisfy industrial applicability. An EPO Board of Appeal said the answer was yes⁵ and the UK courts said no.⁶ Both the EPO and the UK courts apparently believed that a speculative disclosure that turns out to be correct is not sufficient in contrast to the view of Sir Nicholas Pumfrey.

Perhaps the most significant passage in the opinion of Lord Justice Jacob on appeal follows a discussion of Mr. Justice Kitchen's holding at first instance that the specification was speculative:

[133] The Judge thought his conclusion as to the speculative nature of the claims in the patent was confirmed by the subsequent history of investigations by both HGS and others, particularly into B cells and T cells. He set out the detail (which was not challenged) at 141 - 175. His summary is as follows:

"176 The papers and work to which I have referred represent only a very small fraction of the work carried out on Neutrokin- α . Nevertheless, I believe the following general conclusions can be drawn from them and the expert evidence. From 1999 it became increasingly clear that Neutrokin- α is expressed by peripheral blood leukocytes, and in the spleen and lymph nodes. From that time it

⁵ T 0018/09.

⁶ [2010] EWCA Civ 33.

also became apparent that Neutrokin- α plays a significant and particular role in the proliferation and differentiation of B cells. Subsequently it has also been shown to play a part in the regulation of T cell proliferation and activation. As the activities of Neutrokin- α have gradually been elucidated, and particularly those relating to B cells, it has become increasingly recognised as a potential therapeutic target for diseases that are specifically associated with altered B cell function. Notable amongst these are autoimmune diseases such as rheumatoid arthritis and SLE and B cell malignancies such as lymphoma. Neutrokin- α has now been shown to have an important role in the development of autoimmune disease and B cell cancers; but, at the same time, much of its biology remains unclear and is the subject of continuing study by many different research centres. In my judgment the nature and extent of all this research work, the limited conclusions ultimately drawn and the amount of work that remains to be done point strongly to the conclusion that the therapeutic and diagnostic applications suggested in the Patent were indeed speculative."

It seems to be clear from this passage that it was not good enough to set forth applications that might turn out to be true if there was no sound scientific basis for doing so as of the filing date.

APOTEX v. WELLCOME FOUNDATION

Perhaps the leading case discussing speculative disclosures comes from the Supreme Court of Canada, *Apotex Inc. v. Wellcome Foundation Ltd.*,⁷ a case involving the patenting, CP 1,238,277, of a new use for the old drug AZT, the world's first anti-HIV drug. The question for decision by the Court was whether the listed Wellcome inventors were the only inventors of the claimed new use of AZT prior to the priority date, March 16, 1985. The Wellcome inventors were knowledgeable virologists who, when they learned that the HIV was a retrovirus, began to screen compounds that would interfere with a necessary retroviral function. The Court described this work:

11. Once the Glaxo/ Wellcome team had identified suitable compounds, its in-house screening methods were relatively simple. Coating the bottom of a petri dish with murine (mouse) T-cells, the laboratory technician would introduce a retrovirus. Glaxo/ Wellcome used two retrovires found in mice (not humans) because they were readily

⁷ 2002 SCC 77.

reproducible, predictable, reliable and easy to use. Using staining techniques, the laboratory technician could see if the virus spread, destroying the mouse T-cells. If the technician were then to add the candidate "remedial" compound, he or she could see whether the virus triumphed by continuing to kill the T-cells, or the compound triumphed by preserving the T-cells. In November 1984, during Glaxo/ Wellcome's multiple tests of known compounds, the AZT compound produced surprisingly good results, appearing to eradicate completely the retrovirus in the mouse T-cells. It proved more potent than any other compound tested. In argument in this Court, counsel for Glaxo/ Wellcome called this a "eureka moment", but this seems to be something of an exaggeration. There had been no testing in a human cell line (*in vitro*) or in humans (*in vivo*). The object of the exercise was to eradicate HIV in humans, not a mouse virus in a petri dish.

At this point the Court commented that "It seems clear, and was found as a fact by the trial judge, that scientists at Glaxo/ Wellcome and elsewhere recognized that the immune systems of humans and mice are sufficiently different that it is not possible to predict from studies in mouse cells how a drug would work, if at all, in humans." For the Court the question was whether, had an application been filed at this point claiming a method of treating HIV infections, would it have satisfied the utility requirement. The Court indicated that it would not have done so because, although the speculation proved to be correct, it did not believe it appropriate to allow patents for speculative disclosures even when such disclosures ultimately proved to be correct.

But the story does not end here for there were more developments before the March 16, 1985 filing date. NIH had spend a great deal of time and effort to learn about the HIV virus and had developed a sophisticated drug screening technique using a human cell line (ATH8) which could be infected with HIV in vitro to provide information relevant to the ability of a drug to inhibit the replication of HIV in T-cells. This work is described in U.S. Patent No. 4,704,357. Having developed this test, NIH announced that it would test any compound sent to it. As a result Wellcome sent AZT to NIH early in February without identifying the compound as AZT. On February 21, 1985 NIH reported to Wellcome that AZT did inhibit

HIV. Wellcome then disclosed to NIH the identify of the compound around the first of March. Hence NIH had vindicated the Wellcome hunch and at this point there could be little argument that a utility that was not speculative was shown. However, the Court correctly concluded that developing and running the assay to prove that AZT did in fact work did not make the NIH inventors jointly with the Wellcome inventors. As for the doctrine of “sound prediction” the Court explained:

59 The doctrine of sound prediction seems to have had its genesis in a comment by Lord MacDermott in *May & Baker Ltd. & Ciba Ltd.'s Letters Patent, Re (1950)*, 67 R.P.C. 23 (U.K. H.L.), at p. 50 (where, however, he rejected its application on the facts). . . .

60 The doctrine of "sound prediction" was given serious shape and substance by Graham J. in *Olin Mathieson Chemical Corp. v. Biorex Laboratories Ltd.*, [1970] R.P.C. 157 (Eng. Ch. Div.). In that case the proposition was framed as follows, at p. 182:

If it is really possible, according to the evidence, to make a sound prediction about a certain area, then prima facie it would be reasonable that the patentee should have a claim accordingly....

61 The doctrine was explicitly received into our law in *Monsanto, supra*. In that case, the Court was confronted with a patent that included claims to numerous chemical compounds to inhibit premature vulcanization of rubber, but only three of the claimed compounds had actually been prepared and tested before the date the application was filed. The examiner rejected the claims to the untested compounds, holding that "'broad product claims must be adequately supported by a sufficient number of [tested] examples'" (p. 1111). The rejection was upheld by the Patent Appeal Board and the Federal Court, but this Court reversed on the basis that the "architecture of chemical compounds" was no longer a mystery but, within limits, soundly predictable. . . .

66 The doctrine of "sound prediction" balances the public interest in early disclosure of new and useful inventions, even before their utility has been verified by tests (which in the case of pharmaceutical products may take years) and the public interest in avoiding cluttering the public domain with useless patents, and granting monopoly rights in exchange for misinformation.

70 The doctrine of sound prediction has three components. Firstly, as here, there must be a factual basis for the prediction. In *Monsanto* and *Burton Parsons*, the factual basis was supplied by the tested compounds, but other factual underpinnings, depending on the nature of the invention, may suffice. Secondly, the inventor must have at the date of the patent application an articulable and "sound" line of reasoning from which the desired

result can be inferred from the factual basis. In *Monsanto* and *Burton Parsons*, the line of reasoning was grounded in the known "architecture of chemical compounds" (*Monsanto*, at p. 1119), but other lines of reasoning, again depending on the subject matter, may be legitimate. Thirdly, there must be proper disclosure. Normally, it is sufficient if the specification provides a full, clear and exact description of the nature of the invention and the manner in which it can be practised: H. G. Fox, *The Canadian Law and Practice Relating to Letters Patent for Inventions* (4th ed. 1969), at p. 167. It is generally not necessary for an inventor to provide a theory of *why* the invention works. Practical readers merely want to know that it does work and how to work it. In this sort of case, however, the sound prediction is to some extent the *quid pro quo* the applicant offers in exchange for the patent monopoly. Precise disclosure requirements in this regard do not arise for decision in this case because both the underlying facts (the test data) and the line of reasoning (the chain terminator effect) were in fact disclosed, and disclosure in this respect did not become an issue between the parties. I therefore say no more about it.

71 It bears repetition that the soundness (or otherwise) of the prediction is a question of fact. Evidence must be led about what was known or not known at the priority date, as was done here. Each case will turn on the particularities of the discipline to which it relates. In this case, the findings of fact necessary for the application of "sound prediction" were made and the appellants have not, in my view, demonstrated any overriding or palpable error.

72 On March 1, 1985, Glaxo/ Wellcome received from the NIH the key results of the *in vitro* test of AZT against the HIV in a human cell line. This, taken together with Glaxo/ Wellcome's own data on AZT, including the mouse tests, provided a factual foundation. Glaxo/ Wellcome's knowledge of the mechanism by which a retrovirus reproduces, and the "chain terminator effect" of AZT, as disclosed in the patent, was found by the trial judge to provide a line of reasoning by which utility could be established as of the date of the U.K. patent application, March 16, 1985, which is also the priority date by which the invention must be evaluated for purposes of the Canadian patent. Although "sound prediction" was not the precise approach followed by the trial judge, his reasoning as well as his ultimate ruling is entirely consistent with its application.

THE FEDERAL CIRCUIT AND "SOUND PREDICTION"

While not using the expression "sound prediction", the Federal Circuit essentially employed "sound prediction" in *Janssen Pharmaceutica N.V. v. Teva Pharms. USA, Inc. (In re '318 Patent Infringement Litig.)*. The key contribution of the inventor in *Janssen* was her suggestion that a known pharmaceutical, galanthamine, may well be effective in the treatment of Alzheimer's disease, an inspired guess that proved to be true. However, the Federal Circuit believed there was no sound basis for this claimed utility. The Federal Circuit explained:

Janssen's '318 *patent* claims a method for treating Alzheimer's disease with galanthamine. Claim 1 is representative. It claims "[a] method of treating Alzheimer's disease and related dementias which comprises administering to a patient suffering from such a disease a therapeutically effective amount of galanthamine or a pharmaceutically-acceptable acid addition salt thereof." . . . The application for the '318 *patent* was filed on January 15, 1986, by Dr. Bonnie Davis, the claimed inventor.

The specification for the '318 *patent* was only just over one page in length, and it provided almost no basis for its stated conclusion that it was possible to administer "an effective Alzheimer's disease cognitively-enhancing amount of galanthamine." . . . The specification provided short summaries of six scientific papers in which galantamine had been administered to humans or animals. The specification summarized the first paper as showing that administering galantamine with the drug atropine to humans under anesthesia raised blood levels of the hormone cortisol, and the second paper as showing that administering galantamine and atropine together during anesthesia also raised levels of adrenocorticotrophic hormone ("ACTH") in humans. . . . There was no explanation of the significance of increasing cortisol or ACTH levels, but it was known to those skilled in the art in early 1986 that the production of cortisol and ACTH was controlled by the central nervous system rather than the peripheral nervous system, and that the studies thus suggested that galantamine was able to cross the blood-brain barrier and have effects within the brain.

The specification then provided brief summaries of four scientific papers reporting brain effects and positive effects on memory from administering galantamine to animals. . . . The first paper concluded that galantamine intravenously administered to rabbits affected brain wave activity. The second paper concluded that galantamine increased short-term memory in dogs. The third and fourth papers concluded that galantamine reversed amnesia in rats that had been induced by administering the drug scopolamine. The specification did not suggest that such scopolamine-induced amnesia was similar to Alzheimer's disease. The specification did not provide analysis or insight connecting the results of any of these six studies to galantamine's potential to treat Alzheimer's disease in humans.

The specification noted that another prior art scientific paper described an animal testing model for replicating in animals the acetylcholine deficit and other effects of Alzheimer's disease. The specification agreed that acetylcholine deficiency in animals is a "good animal model for Alzheimer's disease in humans" because the deficiency produces "[n]umerous behavioral deficits, including the inability to learn and retain new information." . . . The specification cited the prior art for the conclusion that "[d]rugs that can normalize these abnormalities would have a reasonable expectation of efficacy in Alzheimer's disease." . . . However, the specification did not refer to any then-existing animal test results involving the administration of galantamine in connection with this animal model of Alzheimer's disease.⁸

⁸ 583 F.3d at 1320-22.

Thus the key issue for the Federal Circuit, if we use the language of the Canadian Supreme Court, was whether the patent specification to one of skill in the art provided a sound prediction that galantamine would be effective in treating Alzheimer's disease as of the filing date? On this issue the court concluded that the answer was no explaining:

The utility requirement prevents mere ideas from being patented. As we noted in *Genentech, Inc. v. Novo Nordisk A/S*, . . . , "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. . . . Tossing out the mere germ of an idea does not constitute enabling disclosure." *See also In re Fisher*, . . . (inventions fail to meet the utility requirement if their "asserted uses represent merely hypothetical possibilities, objectives which the claimed [inventions] . . . could possibly achieve, but none for which they have been used in the real world").

The utility requirement also prevents the patenting of a mere research proposal or an invention that is simply an object of research. Again as the Supreme Court stated in *Brenner*, "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." . . . A process or product "which either has no known use or is useful only in the sense that it may be an object of scientific research" is not patentable. . . . As we observed in *Fisher*, inventions do not meet the utility requirement if they are "objects upon which scientific research could be performed with no assurance that anything useful will be discovered in the end." . . . Allowing ideas, research proposals, or objects only of research to be patented has the potential to give priority to the wrong party and to "confer power to block off whole areas of scientific development, without compensating benefit to the public." *Brenner*, . . . (footnote omitted).

Typically, patent applications claiming new methods of treatment are supported by test results. But it is clear that testing need not be conducted by the inventor. In addition, human trials are not required for a therapeutic invention to be patentable. Our predecessor court, the United States Court of Customs and Patent Appeals, held in *In re Krimmel* that patent applications need not "prove that compounds or other materials which [the applicant] is claiming, and which [the applicant] has stated are useful for 'pharmaceutical applications' are safe, effective, and reliable for use with humans." . . . As we observed in *In re Brana*, "[w]ere we to require Phase II testing [human trials] in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue . . . potential cures." . . .

We have held that results from animal tests or in vitro experiments may be sufficient to satisfy the utility requirement. Our predecessor court held in *Krimmel* that animal tests showing that a new nonobvious compound "exhibits some useful pharmaceutical property" are sufficient to demonstrate utility. . . . We noted in *Cross v. Izuka* that "[w]e perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the

[pharmaceutical] compound in question" in order for a patent to issue. . . . We concluded that in vitro test results for a claimed pharmaceutical compound, combined with animal test results for a structurally similar compound, showed "a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence."

In this case, however, neither in vitro test results nor animal test results involving the use of galantamine to treat Alzheimer's-like conditions were provided. The results from the '318 *patent*'s proposed animal tests of galantamine for treating symptoms of Alzheimer's disease were not available at the time of the application, and the district court properly held that they could not be used to establish enablement.

Nor does Janssen contend that the prior art animal testing summarized in the '318 *patent* application's specification established utility. Indeed, both in responding to the examiner's obviousness rejection and in responding to the obviousness defense at trial, the inventor (Dr. Davis) and Janssen's witnesses explicitly stated that the utility of the invention could not be inferred from the prior art testing described in the application.⁹

THE RELATIONSHIP BETWEEN "SOUND PREDICTION", ENABLEMENT AND WRITTEN DESCRIPTION: ARIAD v. ELI LILLY.

An important question for anyone seeking to understand American patent law is why the Federal Circuit, which has now, in its *en banc* decision, *Ariad Pharms., Inc. v. Eli Lilly & Co.*,¹⁰ decided that the United States needed a separate description requirement for originally filed claims in addition to the long established enablement requirement. I suggest in this paper that the answer may be that at least some judges of the Federal Circuit believe that enablement does not include a requirement of a disclosure of a credible utility, i.e. one based on a "sound prediction" in spite of the panel majority decision in *Janssen* and cases cited in support of its decision. Hence, the need to create a separate written description requirement to deal with speculative disclosures that lack a "sound prediction".

⁹ 583 F.3d at 1324-25.

¹⁰ 598 F.3d 1336 (Fed. Cir. 2010)(en banc).

Before turning to *Ariad* itself it is useful to review the key case creating the description requirement for originally filed claims, *University of California v. Eli Lilly & Co.*¹¹ *University of California* involved an early gene patent, U.S. Patent 4,652,525 ('525). The '525 specification clearly described how the inventors had isolated the rat insulin gene, and, based on this method, the inventors included a prophetic example that used the same method to isolate the human insulin gene. Of course not having actually carried out the prophetic example, the inventors could not characterize the gene since they never had actually isolated it. Nevertheless, the application as filed specifically claimed the human insulin gene.

The use of the prophetic example poses two questions. The first is whether the directions of the prophetic example would lead one of skill in the art to the human insulin gene without undue experimentation. Unless the answer is yes the claim is clearly invalid for lack of enablement. The second and more subtle question is whether, even if the answer is yes, there was a credible scientific belief that it would have led to the human insulin gene as of the invention date. In other words it could have been a lucky guess. However, the Federal Circuit indicated that it didn't care whether the inventors had by this prophetic example enabled the human insulin gene since in any event the inventors were not in possession of the human insulin gene. The court explained:

Claim 5 is directed to a recombinant procaryotic microorganism modified so that it contains "a nucleotide sequence having the structure of the reverse transcript of an mRNA of a [human], which mRNA encodes insulin." Thus, the definition of the claimed microorganism is one that requires human insulin-encoding cDNA. The patent describes a method of obtaining this cDNA by means of a constructive example, Example 6. This example, however, provides only a general method for obtaining the human cDNA (it incorporates by reference the method used to obtain the rat cDNA) along with the amino acid sequences of human insulin A and B chains. Whether or not it provides an enabling disclosure, it does not provide a written description of the cDNA encoding human insulin, which is necessary to provide a written description of the subject matter of claim

¹¹ 119 F.3d 1559 (Fed. Cir. 1997).

5. The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.¹²

What is clear is that one did not need to know the nucleic acid sequence of the cDNA in order to use it to make human insulin by inserting it into a vector for insertion into a cell for the purpose of having the cell make human insulin. The purpose or utility of isolating the human insulin gene was to make human insulin from a genetically modified bacteria. Hence, if the specification actually taught how to obtain the human insulin gene, there is no sound reason, assuming novelty and nonobviousness, for not permitting the Genentech inventors to obtain a claim to the isolated human insulin gene unless the prophetic example was speculative. Instead of expressly holding that the prophetic example was speculative as of the filing date, the Federal Circuit created a new requirement, written description for originally filed claims, to invalidate the claim to the human insulin gene. Given that the possession test used by the court required sequencing information, information that only could come from actual experiments, it is possible that the possession test as applied meant that the panel believed that even if the prophetic test was in fact enabling, it was the type of speculation which should not support a patent.

Now we turn to *Ariad Pharmaceuticals* itself. The inventors, many of whom are world famous, made a number of discoveries disclosed in the patent specification including the discover of an important regulatory protein known as NF-kB, many details about this particular

¹² 119 F.3d at 1567.

protein, and most significantly for the claims in suit, methods for controlling it. The patent specification explains these methods of control beginning at column 3, line 54 and ending at column 4, line 28:

The subject invention further relates to methods of regulating (inducing or preventing) activation of NF-KB, controlling expression of the immunoglobulin kappa light chain gene and of other genes whose expression is controlled by NF-kB (e.g., HIV).

As a result of this finding, it is now possible to alter or modify the activity of NF-kB as an intracellular messenger and, as a result, to alter or modify the effect of a variety of external influences, referred to as inducing substances, whose messages are transduced within cells through NF-kB activity. Alteration or modification, whether to enhance or reduce NF-kB activity or to change its binding activity (e.g., affinity, specificity), is referred to herein as regulation of NF-kB activity. The present invention relates to a method of regulating or influencing transduction, by NF-kB, of extracellular signals into specific patterns of gene expression and, thus, of regulating NF-kB-mediated gene expression in the cells and systems in which it occurs.

In particular, the present invention relates to a method of regulating (enhancing or diminishing) the activity of NF-kB in cells in which it is present and capable of acting as an intracellular messenger, as well as to substances or composition useful in such a method. Such methods and compositions are designed to make use of the role of NF-kB as a mediator in the expression of genes in a variety of cell types. The expression of a gene having a NF-kB binding recognition sequence can be regulated, either positively or negatively, to provide for increased or decreased production of the protein whose expression is mediated by NF-kB. NF-kB-mediated gene expression can also be selectively regulated by altering the binding domain of NF-kB in such a manner that binding specificity and/or affinity are modified. In addition, genes which do not normally possess NF-kB binding recognition sequences can be placed under the control of NF-kB by inserting an NF-k binding site in an appropriate position, to produce a construct which is then regulated by NF-kB. As a result of the present invention, cellular interactions between NF-kB and a gene or genes whose expression is mediated by NF-kB activity and which have, for example, medical implications (e.g., NF-kB/cytokine interactions; NF-kB/HTLV-I tax gene product interactions) can be altered or modified.

Turning now to the claims, a representative claim asserted against Lilly's blockbuster drug raloxifene reads:

95 A method for reducing, in human cells, the level of expression of genes which are activated by extracellular influences which induce NF-kB-mediated intracellular signaling, the method comprising reducing NF-kB activity in the cells such that expression of said genes is reduced.

Presumably when a patient ingests raloxifene, it reduces NF-kB activity in her cells which in turn reduces the level of expression of those genes activated by NF-kB. The utility in this case is either for the treatment and prevention of osteoporosis or under certain circumstances for the treatment or prevention of recurrent breast cancer, the FDA approved indications for raloxifene. One can search in vain in the specification for any suggestion of such a use or any suggestion of any use other than one characterized as a medical use as expressed in the following sentence from the previously quoted section of the specification:

As a result of the present invention, cellular interactions between NF-kB and a gene or genes whose expression is mediated by NF-kB activity and which have, for example, *medical implications* (e.g., NF-kB/cytokine interactions; NF-kB/HTLV-I tax gene product interactions) can be altered or modified. (emphasis added).

This is a purely speculative utility and hence claim 95 should have been dismissed immediately as being purely speculative unless the Federal Circuit considers a speculative disclosure that is ultimately shown to be true sufficient for enablement, a belief held by Sir Nicholas Pumfrey, but apparently rejected by the majority of the panel in *Janssen*. In *Ariad* it turns out that there is a medical use for the method. As for enablement even if we accept the prediction that did prove accurate that the inventors' work did have medical implications as sufficient to satisfy the utility requirement, there plainly was no enablement of at least the broad scope of the invention. With respect to enablement the specification had only the following to say beginning on column 37, line 43 and ending at column 38, line 22:

Negative regulation can be effected in an analogous manner. For example, a specific inhibitor molecule which is able to block (reduce or eliminate) NF-kB binding can be added to the biological system in an effective amount. Preferably, this inhibitor is specific for NF-k and does not interact with other cell constituents. An example of such a molecule is I-kB.

Alternatively, negative regulation can be effected using "decoy" molecules, which are

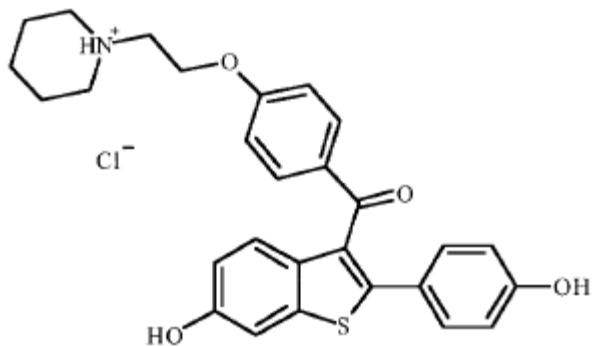
designed to mimic a region of the gene whose expression would normally be induced by NF-kB. In this case, NF-kB would bind the decoy and, thus, not be available to bind its natural target.

Furthermore, in the case of an inhibitor molecule which is also a protein, the gene encoding the inhibitor molecule can be identified, isolated, and cloned into an appropriate expression vector using common methodology. When introduced into an appropriate biological system, the inhibitor molecule is synthesized and functions to interact with NF-kB with its binding site and as a consequence reducing the level of transcription of the gene containing the NF-kB binding site.

Yet another method for negatively regulating the expression of a gene containing an NF-kB binding domain involves the introduction of an effective amount of a decoy sequence encoding the NF-kB binding domain. The decoy sequence serves as an unproductive binding domain with which the NF-kB molecule binds. As the finite number of NF-kB molecules bind to the decoy sequences, the number which bind productively (result in increased transcription) with an intact gene, decreases.

Negative regulation can also be effected by the introduction of "dominantly interfering" molecules (see e.g., Friedman et al., Nature, 335:452-454 (1988)). For example, if the DNA binding domain and the DNA polymerase activating domain of NF-kB are spatially distinct in the molecule, a truncated form of the NF-kB molecule can be synthesized, using well known techniques. A preferred embodiment would be a truncated molecule retaining the DNA binding domain, but lacking the RNA polymerase activating domain. Such a "dominantly interfering" molecule would recognize and bind to the NF-kB binding site, however, the binding would be non-productive. Because the activation portion of NF-kB would be required for enhanced transcription, the truncated molecule would exert no positive effect. Furthermore, its occupation of the NF-kB binding site effectively blocks access to any intact NF-kB molecule which may be present in the cell.

The first suggestion cannot be questioned as it uses the I-kB molecule, the molecule that binds to NF-kB in cells in humans. Hence the specification unambiguously teaches the use of one molecule which has medical implications assuming it could be delivered through injection or in pill form to the cells of the patient. However, there is absolutely no evidence now or at the time of filing that it could be used in any form as a drug. The rest of the possible drugs represent at best a research project. In addition, let us return to raloxifene to show how far away the accused product is from the disclosure. The chemical formula for raloxifene chloride follows:



Raloxifene is an estrogen agonist/antagonist, commonly referred to as a selective estrogen receptor modulator (SERM) that belongs to the benzothiophene class of compounds. Apparently it has been shown to reduce NK-kB activity in some of the cells of the patients. Also according to Ariad one could without undue experimentation have identified raloxifene, but there is no suggestion anywhere that it would have medicinal uses beyond mere speculation. Hence there was no need to invent a new doctrine to deal with the problem of explaining why claim 95 was not patentable unless the fact that the method ultimately has a medical use is sufficient. It would appear therefore that the new possession doctrine (description) for originally filed claims may simply be needed to insure that speculative disclosures cannot be the basis for a valid claim. If this is the case as I believe it is, the Federal Circuit should have simply said so as did the Supreme Court of Canada in *Wellcome* and a panel majority in *Janssen* rather than creating a new, mysterious and unnecessary doctrine called possession (description) for originally filed claims.