TILTING AT THE WINDMILLS OF INHERENCY

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INTRODUCTION

It has long been, and continues to be, a prime objective of biotechnology research to discover new biological properties of chemical compositions, and to exploit these properties to treat and cure disease. Often, research begins with a known chemical composition and a predicted mechanism of biological action, in the expectation that a patent will be awarded to the first to demonstrate a specific use in the treatment of disease. This is entirely consistent with patent law doctrine allowing for patents on new uses of known compositions or processes.* In fact, the increasing rate of biological advancements sustained by pharmaceutical companies around the world is supported largely by revenue generated through the accumulation of patent rights.

Will intellectual property law permit this well established practice to continue? A vociferous dissent by Judge Newman of the United States Court of Appeals for the Federal Circuit ("Federal Circuit"), the specialized appellate court devoted to hearing appeals in patent cases, argues that the court's decision in *Eli Lilly & Co. v. Barr Laboratories, Inc.*, 251 F.3d 955 (Fed. Cir. 2001), severely compromises the ability of pharmaceutical companies to bank on receiving patent protection for the discovery of new biological properties of known chemical compounds and their use to treat disease.

This paper takes a close look at the panel decision and Judge Newman's dissent, and concludes that in this case, Judge Newman, often regarded as providing some of the most analytically sound jurisprudence of the court – especially when it comes to issues affecting biotechnology – has created her own dilemma.

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* *See* 35 U.S.C. §100(b) ("The term 'process' means process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material."). This should not be confused with the patent law axiom that discovery of a new use for an old composition or process cannot resurrect patentability to claims directed to the old composition or process itself. *See In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997).

THE *ELI LILLY & CO. V. BARR LABORATORIES, INC.* CASE

Eli Lilly & Co. v. Barr Laboratories, Inc., 251 F.3d 955 (Fed. Cir. 2001) ("Lilly II"), involved two of the "Prozac" patents owned by Eli Lilly & Co. ("Lilly"), U.S. Pat. Nos. 4,626,549 ("the '549 patent") and 4,590,213 ("the '213 patent"). The somewhat tortured history of this widely followed case begins in 1995. In December of that year, Barr Laboratories, Inc. ("Barr") filed an Abbreviated New Drug Application ("ANDA") with the U.S. Food and Drug Administration, seeking approval to market fluoxetine hydrochloride, the active ingredient in Lilly's drug Prozac, as an antidepressant. *Lilly II*, 251 F.3d at 959. On April 10, 1996, pursuant to 35 U.S.C. § 271(e)(2)(A), Lilly brought an infringement action against Barr, asserting that Barr's ANDA infringed claim 7 of the '549 patent. *Id.* In defense, Barr argued, *inter alia*, that claim 7 of the '549 patent is invalid for obviousness-type double patenting over claim 1 of Lilly's '213 patent. *Id.* at 960.

The double patenting doctrine precludes one patentee from claiming the same invention or obvious variations of the same invention in more than one valid patent. The primary purpose of the judicially created doctrine of obviousness-type double patenting is to prevent a patentee from extending the patent monopoly past the statutorily limited term by obtaining claims in a later patent to subject matter that is the same as, or merely an obvious variation of, subject matter claimed in an earlier patent. *See*, *e.g.*, *Applied Materials Inc. v. Advanced Semiconductor Materials America, Inc.*, 98 F.3d 1563, 1577 (Fed. Cir. 1996) (Archer, C.J., concurring-in-part and dissenting-in-part).

On cross motions for summary judgment, the United States District Court for the Southern District of Indiana held the '549 patent was not invalid for obviousness-type double patenting. *Lilly II*, 251 F.3d at 959. Barr appealed to the Federal Circuit, which reversed the district court's finding, holding claim 7 of the '549 patent invalid for obviousness-type double patenting over claim 1 of U.S. Patent No. 4,018,895, another Lilly patent, and not reaching the double patenting argument based on the '213 patent. *Eli Lilly & Co. v. Barr Laboratories, Inc.*, 222 F.3d 973, 985-988 (Fed. Cir. 2000) ("Lilly I").

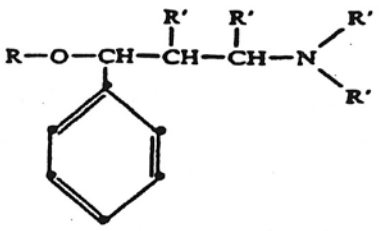
The Federal Circuit then granted Lilly's motion for rehearing *en banc*, and the *en banc* court vacated the panel's opinion in *Lilly I*, sending the case back to the panel for a specific revision of the double patenting section. *Lilly II*, 251 F.3d at 972. The Federal Circuit panel's recent decision on May 30, 2001 again reverses the district court's finding that claim 7 of the '549 patent was not invalid for obviousness-type double patenting, this time holding that claim 7 of the '549 patent is invalid for double patenting over claim 1 of Lilly's '213 patent. *Id.*

THE FEDERAL CIRCUIT'S ANALYSIS

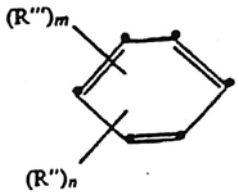
In *Lilly II*, the Federal Circuit panel explained that analysis under the double patenting doctrine involves two steps. First, the court construes the claims in the earlier and later patents and determines the differences, if any, between the claims. Next, to the extent the claims do indeed differ, the court determines whether the differences between the claims are sufficient to render the claims "patentably distinct." *Id.* at 968. Drawing on statutory novelty and non-obviousness doctrines, the Federal Circuit explained that a patent claim is not patentably distinct from an earlier patent claim if the later claim is obvious over, or anticipated by, the earlier claim. *Id.* Thus, where an earlier issued claim anticipates or renders obvious a later claim, the later claim is not patentably distinct from the earlier claim and is therefore invalid under the double patenting doctrine. To reach a contrary conclusion would allow a patentee to extend the patent monopoly past the statutorily limited term by obtaining successive patents on the same basic subject matter and would frustrate one of the fundamental principles of the patent system, namely, that when the right to exclude granted by a patent expires at the end of the patent term, the public is free to use the invention as well as variations of the invention that are obvious to one of ordinary skill in the relevant art. *See* 3 Donald S. Chisum, *Chisum on Patents* § 9.01, at 9-3 to 9-4 and § 9.03[3][a], at 9-66 (1995).

Turning to the claims in the Lilly patents, claim 4 of the '549 patent recites:

> A method of blocking the uptake of monoamines by brain neurons in animals comprising administering to said animal a monoamine blocking amount of a compound of the formula



> wherein each R′ is independently hydrogen or methyl; wherein R is naphthyl or



> wherein R″ and R‴ are halo, trifluoromethyl, C_1 -C_4 alkyl, C_1 -C_3 alkyloxy or C_3 -C_4 alkenyl; and wherein n and m are 0, 1 or 2; and acid addition salts thereof formed with pharmaceutically-acceptable acids.

Claim 7 of the '549 patent, which depends from claim 4, specifically claims blocking the uptake of the monoamine serotonin in an animal's brain neurons through administration of the compound N-methyl-3-(p-trifluoromethylphenoxy)-3-phenylpropylamine hydrochloride -- commonly referred to as fluoxetine hydrochloride.*

Claim 1 of the '213 patent recites:

> A method for treating anxiety in a human subject in need of such treatment which comprises the administration to said human of an effective amount of fluoxetine or norfluoxetine or pharmaceutically acceptable salts thereof.

As analyzed by the Federal Circuit panel, "the only difference between claim 1 of the '213 patent and claim 7 of the '549 patent is that the former addresses a method of treating anxiety in humans with fluoxetine hydrochloride while the latter claims a method of using fluoxetine hydrochloride to block serotonin uptake in animals." *Lilly II*, 251 F.3d at 969.

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* Dependent claim 7 of the '549 patent depends from dependent claim 6, which in turn depends from dependent claim 5, which in turn depends from independent claim 4. These claims are set forth below. Because a dependent claim includes all the limitation of the independent claim from which it eventually depends and any intervening claims, 35 U.S.C. §112, claim 7 is directed specifically to blocking the uptake of serotonin by administering fluoxetine hydrochloride.

5. A method according to claim 4 wherein the monoamine to be blocked is serotonin.

6. A method according to claim 5 employing N-methyl-3-(p-trifluoromethylphenoxy)-3-phenylpropylamine or a pharmaceutically-acceptable acid addition salt thereof.

7. The method of claim 6 employing N-methyl-3-(p-trifluoromethylphenoxy)-3-phenylpropylamine hydrochloride.

However, the court's analysis continued, the evidence proffered by Barr proved that inhibiting serotonin uptake is an inherent property of fluoxetine hydrochloride upon administration, i.e., "a natural biological activity that occurs when fluoxetine hydrochloride is administered." *Id.* Thus, claim 1 of the '213 patent – claiming a method of treating anxiety with fluoxetine hydrochloride – anticipates claim 7 of the '549 patent – claiming a method of using fluoxetine hydrochloride to block serotonin uptake – because the administration of fluoxetine to treat anxiety as per claim 1 of the '213 patent would inherently block serotonin uptake. *Id.* Therefore, the court concluded, since claim 1 of the '213 patent anticipates claim 7 of the '549 patent, the latter is not patentably distinct from the former and is therefore invalid for double patenting. *Id.* at 970-971.

JUDGE NEWMAN'S CRITICISM

In a separate opinion, styled a "dissent[] from the refusal to reconsider the case en banc," *Lilly II*, 251 F.3d at 972, Judge Newman offered sharp criticism of the panel's decision that "discovery of a new and unobvious biological property is unpatentable because it is inherent in the chemical compound." *Id.* at 976. Judge Newman explained, "every biological property is a natural and inherent result of the chemical structure from which it arises, whether or not it has been discovered. To negate the patentability of a discovery of biological activity because it is 'the natural result' of the chemical compound can have powerful consequences for the patentability of biological inventions." *Id.*

Evidently, Judge Newman was concerned that the panel's decision, and the *en banc* court's refusal to reconsider the case, heralded a new rule of patentability for biological inventions and that this new rule would preclude patentability for the discovery of "new and unobvious biological propert[ies]" which are inherent in the chemical compounds from which they arise. Predictably, this would have a major chilling effect on both the revenue streams and the future research efforts of biotechnology and pharmaceutical companies.* Thus, Judge Newman's dissent has sparked a wave of concern among researchers in the biotechnology community as well as patent counsel responsible for protecting their inventions.

However, as we show below, Judge Newman's prediction that the panel's decision spells an end to the patentability of biological inventions is unfounded. Instead, the panel's decision is both an accurate and necessary application of traditional patent law doctrine and researchers can rest assured that it does not jeopardize the patentability of new and unobvious biological properties or new uses for known compounds.

* The day after the Federal Circuit handed down its decision in *Lilly I*, invalidating claim 7 of the '549 patent, Eli Lilly & Co. shares lost almost a third of their value, dropping $33.56 to $75 from a high of over $108.

ANALYSIS OF THE PANEL'S DECISION

In many respects, the Federal Circuit panel's decision that claim 1 of the '213 patent anticipates claim 7 of the '549 patent and, therefore, that the latter is not patentably distinct from the former, is based on a standard application of anticipation by inherency. Under the doctrine of anticipation by inherency, "[i]f the prior art reference does not expressly set forth a particular element of the claim, that reference may still anticipate if that element is 'inherent' in its disclosure. To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, *and that it would be so recognized* by persons of ordinary skill.'" *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (emphasis added); *see also Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999); *Abbott Laboratories v. Geneva Pharmaceuticals, Inc.*, 182 F.3d 1315 (Fed. Cir. 1999).

In the *Lilly II* case, claim 1 of the '213 patent disclosed every limitation of claim 7 of the '549 patent, with the exception of the "blocking the uptake of monoamines . . . wherein the monoamine to be blocked is serotonin" limitation. Thus, if it were shown that blocking serotonin uptake was "necessarily present" in the disclosure of claim 1 of the '213 patent *and that this would be recognized* by one of ordinary skill in the art, claim 1 of the '213 patent would inherently anticipate claim 7 of the '549 patent. Barr presented a "panoply" of evidence on these points, persuading the panel that fluoxetine hydrochloride both necessarily inhibits serotonin uptake upon administration and that this property would be recognized by one of ordinary skill in the art. *Lilly II*, 251 F.3d at 969-970. This made out a prima facie case of inherent anticipation. Because the panel found claim 1 of the '213 patent inherently anticipates claim 7 of the '549 patent, it necessarily followed that claim 7 of the '549 patent is not patentably distinct from claim 1 of the '213 patent and therefore, that the '549 patent's claim 7 is invalid for double patenting over the '213 patent's claim 1. As explained above, where an earlier issued patent claim anticipates a later claim, the later claim is not patentably distinct from the earlier claim and is therefore invalid under the double patenting doctrine. *Id.* at 970; *see also In re Goodman*, 11 F.3d 1046, 1053 (Fed. Cir. 1993) (absent a terminal disclaimer, genus claims were properly rejected under the doctrine of obviousness-type double patenting over species claim, because claim to species would anticipate claims to genus). Importantly, in order to support its holding of inherent anticipation the panel necessarily found not only that "serotonin uptake inhibition is an inherent property of fluoxetine hydrochloride," but also that the evidence proffered by Barr "support[s] the *recognition* of this inherent biological function of fluoxetine hydrochloride." *Lilly II*, 251 F.3d at 969 (emphasis added).*

* It is also important to realize that the panel's conclusion that claim 7 of the '549 patent is inherently anticipated by claim 1 of the '213 patent, and therefore invalid for double patenting, does not depend on the principle that the anxiolytic effects of fluoxetine hydrochloride, claimed in claim 1 of the '213 patent, are *caused* by the serotonin uptake blocking properties of fluoxetine hydrochloride. For example, even if the anxiolytic effects of fluoxetine hydrochloride were caused by a separate mechanism of action – perhaps by stimulated serotonin production, by blocking dopamine uptake, or

Thus, Judge Newman's criticism of the panel decision on the ground that it would preclude patentability for the discovery of "new and unobvious biological propert[ies]" is misplaced. The panel's decision reveals its conclusion that the relevant property of fluoxetine hydrochloride – inhibiting serotonin uptake upon administration – was neither new nor nonobvious. Had this property been new or nonobvious, the panel could not have reached the legal conclusion of inherent anticipation. As explained above, inherent anticipation requires not only that fluoxetine hydrochloride actually and necessarily inhibit serotonin uptake, but also that one of ordinary skill in the art would *recognize* this. By concluding fluoxetine hydrochloride "inherently" blocks serotonin uptake, the panel necessarily found that one of ordinary skill in the art would recognize this serotonin uptake blocking property of fluoxetine hydrochloride, and therefore, implicitly, if not explicitly, acknowledged this property is not new or nonobvious.

The language of Judge Newman's dissent illustrates the inaccuracy that led her astray. In her dissent, Judge Newman asserted "every biological property is a natural and inherent result of the chemical structure from which it arises, *whether or not it has been discovered*." While Judge Newman's usage of "inherent" may comport with a simple English definition of the word it most certainly does not meet the legal definition of inherency, which requires not only that the property be necessarily present, but also that it be *recognized* as such by one of ordinary skill in the art. Judge Newman herself has reiterated this definition of inherency on numerous occasions, explaining that "[t]o serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Continental Can Co. U.S.A., Inc., v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991) (Newman, J.); *see also In re Schreiber*, 128 F.3d 1473, 1481 (Fed Cir. 1997) (Newman, J., dissenting) ("An inherent disclosure, to be invalidating as an 'anticipation,' is a disclosure that is necessarily contained in the prior art, and would be so recognized by a person of ordinary skill in that art. 'Inherency' charges the inventor with knowledge that would be known to the art, although not described. Inherency is not a matter of hindsight based on the applicant's disclosure: the missing claim elements must necessarily be present in the prior art.") (internal citations omitted). In the *Lilly II* case, had the serotonin uptake blocking property of fluoxetine hydrochloride not been recognized by those of ordinary skill in the art, presumably even the panel would agree that it would not constitute an "inherent" property for purposes of patent law anticipation.

Similarly, the panel's decision is in complete accord with patent law doctrine allowing the patentability of new uses for known compositions or processes. *Bristol-Myers Squibb Co. v.*

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even by placebo effect – so long as the administration of fluoxetine hydrochloride necessarily inhibits serotonin uptake – even collaterally – and so long as this is recognized by those of ordinary skill in the art, claim 7 of the '549 patent would presumably be inherently anticipated by, and therefore invalid for double patenting over, claim 1 of the '213 patent.

Ben Venue Laboratories, Inc., 246 F.3d 1368, 1376 (Fed. Cir. 2001). As explained above, the panel's legal conclusion of inherent anticipation denotes that employing fluoxetine hydrochloride to block serotonin uptake was a known and recognized use, not a new use. Claim 7 did not claim any use for fluoxetine hydrochloride other than blocking serotonin uptake. Thus, Claim 7 of the '549 patent, invalidated by the panel's decision, did not claim a *new* use of fluoxetine hydrochloride. The panel never suggests that claims directed to truly new uses of fluoxetine hydrochloride would be unpatentable over claim 1 of the '213 patent, even if the new use operates by the mechanism of serotonin uptake inhibition. For example, if Lilly were to file a patent application tomorrow claiming a method for treating warts comprising the administration of a therapeutically effective dose of fluoxetine hydrochloride, assuming this use of fluoxetine hydrochloride has not been already recognized in the art, the panel decision does not preclude the patentability of this claim, even if the mechanism by which the fluoxetine hydrochloride treats warts is through serotonin uptake inhibition. To the extent this hypothetical claim remains patentable over the '213 patent, it is precisely because it claims a new use – i.e., one not recognized by those of ordinary skill in the art – in marked contrast to claim 7 of the '549 patent. Therefore, any apprehension that the panel's decision somehow sounds a death knell for the patentability of new uses for known chemical compositions is illusory.

To the extent Judge Newman disagrees with the panel's conclusion that the evidence in *Lilly II* sufficed to demonstrate the serotonin blocking property of fluoxetine hydrochloride was both necessarily present *and recognized* in the art, the disagreement centers narrowly on the record of *Lilly II* and offers no suggestion of a cataclysmic change in the rules of patentability for biological inventions. As this paper has shown, biotechnology researchers and their patent counsel can rest assured that the phantoms Judge Newman perceives in the panel decision will not materialize to haunt them.

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