WEST/CRS

Nos. 02-1052, -1065

United States Court Of Appeals
for the
Federal Circuit

Integra LifeSciences I, Ltd. And The Burnham Institute,
Plaintiff-Cross Appellants,
And

Telios Pharmaceuticals, Inc.,
Plaintiff-Appellee,

FILED
U.S. COURT OF APPEALS FOR
THE FEDERAL CIRCUIT
OCT 24 2005
10/24/05
JAN HORBALY
CLERK

v.
Merck KGaA,
Defendant-Appellant,

and

The Scripps Research Institute and Dr. David A. Cheresh,
Defendants.

APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE SOUTHERN DISTRICT OF CALIFORNIA IN CASE 96CV-1307 JMF
JUDGE JAMES FITZGERALD

BRIEF OF AMICUS CURIAE BAVARIAN NORDIC A/S

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October 24, 2005

QUESTION PRESENTED

Whether § 271(e)(1)'s statutory text and legislative purpose continue to impose substantial limitations on the applicability of that statute's safe harbor provision in the wake of the U.S. Supreme Court's opinion in *Merck v. Integra*, 125 S. Ct. 2372 (2005).

CERTIFICATE OF INTEREST

Pursuant to Local Circuit Rules 47.4 and 26.2A and Rule 26.1 of the Federal Rules of Appellate Procedure, counsel for Bavarian Nordic A/S certifies the following:

1. The full name of every party represented by the undersigned is:

Bavarian Nordic A/S

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by the undersigned is:

Not Applicable (real party in interest is Bavarian Nordic A/S)

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party represented by the undersigned is:

None

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court are:

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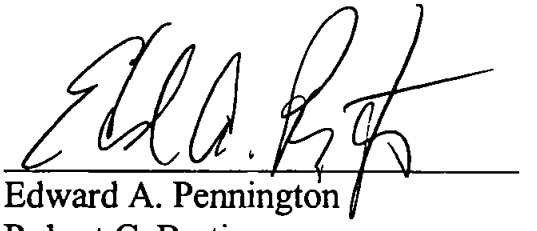

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INTEREST OF THE *AMICUS*

Founded in 1994, Bavarian Nordic A/S ("Bavarian Nordic") is a leading international biopharmaceutical company developing, producing, and marketing innovative vaccines to prevent and treat infectious diseases and cancer. With operations in Denmark, Germany, and the USA, Bavarian Nordic holds a number of U.S. and foreign patents.

Bavarian Nordic's product line includes a new generation smallpox vaccine, marketed under the brand name IMVAMUNE, which has achieved worldwide acclaim for being much more safe and effective than existing smallpox vaccines. While smallpox was thought to be eradicated, the threat of bioterrorism has generated intense interest in the United States to stockpile an effective smallpox vaccine as a component of Homeland Security.

Bavarian Nordic developed its smallpox vaccine technology and products well before the terror threats posed after September 11, 2001. This focus on safe vaccine development has prevailed notwithstanding that the pool of vaccine producers otherwise decreased over the past 20 years, with pharmaceutical companies transitioning to more profitable and less challenging healthcare areas. In view of a potential terror attack, however, the lack of vaccine stockpile and reluctance from so-called first line responders to use the traditional smallpox vaccine recently prompted a need for a safer vaccine.

SUMMARY OF ARGUMENT

The U.S. Supreme Court's opinion in *Merck v. Integra* clarified -- and potentially expanded -- the scope of infringing conduct eligible for protection under § 271(e)(1)'s safe harbor. *Merck*, however, presented a narrow set of facts to the Supreme Court, and as required by the statute's language, this Court should continue to apply a rigorous test to determine whether infringing activities are "solely" for the use of developing information for the regulatory process, particularly in cases where infringing products have substantial economic value prior to formal regulatory approval. In such cases, courts must be particularly wary to ensure that the infringing use is limited in scope and proportionality to regulatory needs.

ARGUMENT

The U.S. Supreme Court's recent opinion in *Merck v. Integra*, 125 S. Ct. 2372 (2005), potentially expanded the scope of activity that may be deemed "reasonably related to the development and submission of information" under 35 U.S.C. § 271(e)(1). The section's applicability, however, remains subject to several significant limitations not implicated by the facts considered by the Supreme Court. In setting guidelines for the interpretation of § 271(e)(1), this

Court should thus proceed cautiously, and construe the *Merck* opinion narrowly within the context of these limitations. Below, this brief first addresses the Supreme Court's limited holding in *Merck*, and then proceeds to address two major considerations that should continue to limit the breadth of § 271(e)(1).

I. THE SUPREME COURT'S *MERCK* OPINION IS LIMITED TO AN INTERPRETATION OF THE WORDS "REASONABLY RELATED" AND "INFORMATION" IN THE § 271(e)(1) CONTEXT.

The Supreme Court's *Merck* opinion ostensibly expands the protection afforded by § 271(e)(1), but the opinion's applicability is not as broad as its language suggests. In interpreting whether otherwise infringing activity might be "reasonably related" to the development of "information" within the context of the statute, the *Merck* Court addressed three questions: (1) whether § 271(e)(1)'s scope is limited to clinical studies; (2) whether § 271(e)(1)'s scope in pre-clinical studies is limited to determinations of a product's safety; and (3) whether § 271(e)(1)'s scope is limited to uses of patented compounds that actually result in the submission of information to the FDA. *See generally Merck*, 125 S. Ct. 2372 (2005). The Court answered each of these questions in the negative. *Id.*

The Court first determined that "§ 271(e)(1)'s exemption from infringement extends to all uses of patented inventions that are reasonably related to the development and submission of *any* information under the FDCA." *Id.* at 2380

(original emphasis). The Court reasoned that no verbiage in the statute particularly limited either "the phase of research" in which a use of the invention must occur or the "particular submission" within which any resulting information must be applied. *Id.* In addition, because information related to drug efficacy, mechanism of action, pharmacokinetics, and pharmacology are relevant to the FDA's "comparison of the risks and benefits associated with...proposed clinical trials," all such information was deemed to be properly within the scope of § 271(e)(1). *Id.* at 2381.

The Court proceeded to identify the appropriate time-frame for determining whether use of a patented compound is "reasonably related to the development and submission of information" to the FDA. *Id.* at 2382-2384. The Court determined that the § 271(e)(1) reasonableness inquiry ought to be conducted at the time when the experiment is to be conducted, rather than after the fact. Even failed experiments, the Court reasoned, may be entitled to § 271(e)(1)'s safe harbor if at the time they were conducted they were reasonably related to the regulatory approval process. *Id.* at 2383 ("Properly construed, § 271(e)(1)'s safe harbor leaves adequate space for experimentation and failure on the road to regulatory approval.").

While the Court has thus rendered broad interpretations of "reasonably related" and "information," the issues actually addressed by the Court were quite

narrow. The case, as it came before the Court, did not implicate the statutory limitations intended to ensure § 271(e)(1)'s narrow application in the service of fair and efficient competition. Rather, *Merck* implicated only the threshold question of whether infringing activities fall within the statute's ambit.

While § 271(e)(1) requires that acts be "reasonably related to the development and submission" of qualifying information in order to come under the aegis of the statute, it is not enough *merely* that there be a reasonable relationship to such information. Rather, to invoke the statute's protection, the infringing act must also be conducted "solely" in pursuance of such information. *See* 35 U.S.C. § 271(e)(1). In addition, the Court expressly declined to consider whether the particular *variety* of patent infringed might negate § 271(e)(1)'s applicability. *See Merck*, 125 S. Ct. at 2382 n.7 ("We therefore need not -- and do not -- express a view about whether, or to what extent, § 271(e)(1) exempts from infringement the use of 'research tools' in the development of information for the regulatory process."). As such, the Court's opinion in *Merck* addresses only the question of what uses are potentially *eligible* for § 271(e)(1) protection, not whether such protection is ultimately *warranted*.

II. THE SUPREME COURT'S *MERCK* OPINION DOES NOT ABROGATE OTHER STATUTORY LIMITATIONS ON § 271(e)(1)'S APPLICABILITY

Section 271(e)(1) is not a model of clarity. *See Eli Lilly & Co. v. Meditronic, Inc.*, 496 U.S. 661, 679 (1990) ("No interpretation we have been able to imagine can transform § 271(e)(1) into an elegant piece of statutory draftsmanship.") Courts to consider the question have generally agreed that a primary purpose of the section was to facilitate a competitive market for pharmaceuticals, minimizing the barrier to entry effected by the patent system's intersection with the regime of pharmaceutical regulation. *See Eli Lilly*, 496 U.S. at 670 ("the combined effect of the patent law and the premarket regulatory approval requirement was to create an effective extension of the patent term. . . . The 1984 Act sought to eliminate this distortion. . ."); *see also Intermedics v. Ventritex, Co.*, 775 F. Supp. 1269, 1272-73 (N.D. Cal. 1991) (same). As the court in *Intermedics* recognized, § 271(e)(1) represented Congress' preference for fair and efficient competition over the effective extension of monopoly interests. *See Intermedics*, 775 F. Supp. at 1276-77 ("Congress elevated the health care interests of the public above the pecuniary interests of the patent holders."). As such, where the terms of § 271(e)(1) are not self-defining, the statute ought to be interpreted as in the service of fair competition.

A. Where Compliance with the Regulatory Process is Confounded with a Realistic Potential for Unfair Profit, § 271(e)(1) Limits Infringing Activities "Solely" to Uses Reasonably Necessary for Regulatory Compliance.

Section 271(e)(1)'s applicability is limited primarily by the statute's insistence that only infringing activities conducted "solely" for use in regulatory compliance are entitled to its safe harbor. *See* 35 U.S.C. § 271(e)(1). This Court has noted that "[t]he term 'solely' places a constraint on the inquiry into the limits of the exemption. The exemption *cannot extend at all* beyond uses with the reasonable relationship specified in § 271(e)(1)."). *Integra Lifesciences I, Ltd. v. Merck KGaA*, No. 02-1052, -1065, 2003 U.S. App. LEXIS 27796, at *14 (Fed. Cir. July 10, 2003) (emphasis added). As the issues determined by the Supreme Court did not confront the "solely" prong of the § 271(e)(1) inquiry, this Court's rigorous interpretation of that constraint remains vital in the wake of *Merck.*

In the instant case, the defendants' allegedly infringing use of Integra's RGD peptide patents poses few risks to fair competition, because any anti-angiogenic therapy Merck ultimately develops will be unmarketable until it receives FDA approval, and once such approval is attained § 271(e)(1)'s safe harbor will expire. The situation is quite different, however, where infringements of the patented invention can directly enter the market prior to formal regulatory approval.

Smallpox vaccine is one example of a product within § 271(e)(1)'s foreseeable ambit that has considerable market value even prior to FDA approval. To illustrate, the National Institutes of Health recently issued a Request for Proposals (RFP-DHHS-ORDC-V&B-05-06) to supply the government with

millions of doses of modified Vaccinia Ankara virus (MVA)-based smallpox vaccine despite the fact that no MVA-based vaccine has as yet received FDA approval. This contract, when issued, has an expected value of approximately $1 billion.

As distinguished from the facts in *Merck*, smallpox vaccine implicates serious economic concerns relevant to § 271(e)(1)'s applicability. Section § 271(e)(1) requires more than a mere nexus to the regulatory process. Clearly, commercial sales of large quantities of pharmaceuticals in parallel with the regulatory approval process would not be within the ambit of protection of § 271(e)(1), even if the sales were occurring simultaneously with clinical trials. In such circumstances, Congress' concern for fair competition would be turned on its head. While smallpox vaccine presents only one specific example, many other drugs and vaccines may be developed for federal government contracts under the BioShield Program, for which FDA approval is unnecessary for at least a portion of the pharmaceutical's commercial life. In these cases, protecting intellectual property rights is commensurate with protecting national security. In order to ensure that inventors have the incentive to innovate and advance in such a critical area, it is essential to preserve the vitality of patent rights.

The Supreme Court in *Merck* considered the question of when research may be "reasonably related" to the regulatory process, but did not address when an

infringing use is "solely" for such uses. In cases where a compound or device has economic value prior to FDA approval, the infringement of a patented invention will likely not be *solely* for regulatory use.[1]

While this Court does not -- and should not -- base the applicability of § 271(e)(1) on its impressions of a defendant's subjective motives, an objective test should limit § 271(e)(1)'s applicability where regulatory purposes are confounded with the potential for unfair profit. *See Intermedics,* 775 F. Supp. at 1278 ("Congress intended the 'test' for determining whether the exemption has been lost to be 'objective' rather than 'subjective.'"). In applying this test, the burden should remain with the accused infringer to prove that infringing activities are commensurate both in their scope and in their degree to legitimate regulatory needs. For example, where infringing products are created for testing, the infringer should be required to prove that the quantity of infringing products does not exceed what is reasonably necessary for FDA purposes. Neither § 271(e)(1) nor the

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[1] This discussion concerns only those situations -- such as the sale of smallpox vaccine prior to regulatory approval -- where the infringing activity is *itself* unfairly competitive. As such, it is distinguishable from the situation in *Intermedics*, where the defendant's economic activities were not themselves infringing. *See Intermedics,* 775 F. Supp. at 1279 ("Congress clearly intended . . . to create a legal environment in which the potential competitors of patent holders would be free, through non-infringing activities like raising capital, to position themselves to enter the market in a commercially significant way just as soon as the relevant patents expired.").

Supreme Court's *Merck* opinion authorizes an infringer to reap unjust economic enrichment during the life of a valid patent.

B. Infringing Use of "Research Tools" May Not Be "Reasonably Related" to the Regulatory Process, as Required by § 271(e)(1), But Other Cases May Present Better Facts for Considering the Scope of a "Research Tools Exception."

A specific application of § 271(e)(1)'s requirement that infringing acts be limited in scope and proportionality to the needs of the regulatory regime involves § 271(e)(1)'s applicability to "research tools." This Court has already expressed concern that "exaggerating § 271(e)(1) out of context would swallow the whole benefit of the Patent Act for some categories of biotechnological inventions." *See Integra Lifesciences*, 2003 U.S. App. LEXIS 27796, at *19. Section 271(e)(1), this Court noted, was not intended "to deprive entire categories of inventions of patent protection." *Id.*

The Supreme Court, in footnote 7 of its *Merck* opinion, declined to consider the applicability of a "research tools" exception to this case, noting that "Respondents have never argued the RGD peptides were used at Scripps as research tools, and it is apparent from the record that they were not." *Merck*, 125 S. Ct. at 2382 n.7. Yet the inclusion of footnote 7 suggests a tension with the broad language encountered earlier in the opinion, where the Court expresses, "we think it apparent from the statutory text that § 271(e)(1)'s exemption from

infringement extends to *all uses of patented inventions . . . .*" *Id.* at 2380 (emphasis added). To the extent that the Court pulls back, in footnote 7, from its earlier broad pronouncement, it suggests that the Court is motivated by concerns of scope and proportionality inherent in the "reasonably related" language of the statute. For example, use of a general purpose computer may be necessary in the process of testing pharmaceuticals, but the infringing use of a general patent on the computer's technology would be well beyond the scope of what is "reasonably related" to compliance with FDA regulations. Thus, the Supreme Court, in recognizing the possibility of a research tools exception, suggested that what is "reasonably related" to the regulatory process may have substantial limits.

At present, however, there is no clear definition for what constitutes a "research tool," and the facts of the instant case are unlikely to offer guidance. As such, this Court should decline to address the research tools question at this time. Indeed, fact patterns more squarely implicating the infringement of "research tools" will likely come before this Court sooner rather than later. In the wake of *Merck*, it has been suggested that pharmaceutical researchers will broadly breach their licensing agreements with holders of research tool patents. *See* Stephen B. Maebius & Harold C. Wegner, Merck v. Integra*: The Impact of a Broader "Safe Harbor" Exemption on Nanobiotechnology*, 2(3) Nanotech. L. & Bus. J. 1 (2005):

> Pharmaceutical companies may be emboldened by the *Merck* decision to reevaluate current licenses under which they are paying royalties to

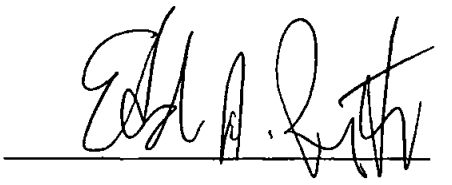
> the owner of a nanotech research tool patent holder. In the case of an existing license. . .the licensee might claim that their activities are now protected under the safe harbor and therefore do not require a license.

See also Stanton J. Lovenworth & Melissa P. Cohen, *The Research Tool Connundrum: 'Merck' decision leaves open questions on boundaries of safe harbor*, N.Y.L.J., Oct. 17, 2005, at S4, S10 ("many pharmaceutical companies may be willing to use patent research tools without a license while the research tool industry is left wondering what value remains in their patents."). Such cases will provide this Court with a more appropriate context for considering the research tools issue. In any event, as the Supreme Court has recognized, the facts before this Court do not properly implicate "research tools," and this Court should similarly decline to broach the issue.

CONCLUSION

For the foregoing reasons, this Court should continue to find that § 271(e)(1)'s applicability is limited to uses solely related to compliance with the pharmaceutical regulatory regime. Particularly where inventions have significant economic value prior to formal regulatory approval, this Court should insist that the scope and proportionality of infringing use be commensurate to regulatory needs. The Supreme Court's *Merck* opinion does not vitiate a patent holder's right to be free from unfair competition.

Respectfully submitted,



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Dated: October 24, 2005

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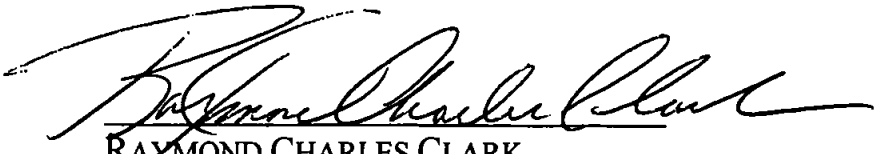

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