In a patent infringement suit closely watched by many connected to the biotechnology and pharmaceutical industries, the United States Supreme Court recently issued a unanimous decision in *Merck KGaA v. Integra LifeSciences I, Ltd.*, No. 03-1237, (S.Ct. June 13, 2005). The decision broadly interprets the scope of the Patent Act’s safe harbor exemption from patent infringement to include certain preclinical research and development activities, whether or not ultimately the subject of an FDA submission, “as long as there is a reasonable basis for believing that the experiments will produce ‘the types of information that are relevant to an IND [Investigational New Drug application] or NDA [New Drug Application]’. Slip Opinion at 14 (quoting the Brief of the United States as Amicus Curiae). The Court, however, specifically declined to address an issue of interest to many in the biotechnology community: whether or not the exemption applies to infringement of patents relating to research tools in the development of information for FDA submissions.

The case arose when the patent owners, Integra Lifesciences and the Burnham Institute, filed a patent infringement suit against Merck KGaA and others, alleging that research funded by Merck infringed the Integra patents. The research involved the use of various compositions, including components and methods covered by the Integra patents, in a procedure shown to reverse tumor growth in chick embryos.

Based on the success of that research, Merck agreed to expand the research to develop a similarly acting drug for humans, with a view toward eventually submitting an IND to the FDA. In defense, Merck argued, among other things, that it was exempt from infringement under a safe harbor provision of the Patent Act that allows research where information is to be submitted to the FDA. The Integra compositions were not ultimately the compositions chosen for the IND submission, but they were used as positive controls in the research. The District Court and the Court of Appeals for the Federal Circuit ruled in the patent owners’ favor, finding infringement and holding that Merck’s activities did not fall within the exemption. Merck sought Supreme Court review, setting the stage for the Court’s consideration of the statutory exemption, Patent Act Section 271(e)(1).

Under Section 271(a) of the Patent Act, 35 U.S.C. et seq., it is generally an act of patent infringement to “mak[e], us[e], offer to sell, or sell within the United States or import into the United States a patented invention … solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products. (Emphases added).

A principal component of the federal framework requiring submission of information relating to the...
manufacture, use, or sale of drugs is the Federal Food, Drug, and Cosmetic Act (FDCA). Under the FDCA, drug manufacturers must request FDA approval to perform human clinical trials by submitting an investigational new drug application (IND). The IND must describe preclinical testing of the drug that is “adequate to justify the proposed clinical testing.” Also, before FDA will authorize a manufacturer to market a new drug, the manufacturer must submit a new drug application (NDA) to FDA, which must include results of investigations that have been performed to determine whether or not a drug is safe and effective in use. An NDA must include all clinical studies, and also must provide any preclinical studies showing the efficacy, toxicity, and pharmacological properties of the drug.

The Hatch-Waxman Act, as the statutory title suggests, was intended, in part, to speed to market competitive drugs by allowing some research using the patented inventions of another during the patent term. The commercial manufacture and sale of a drug thus developed, however, can not legitimately occur until after the relevant patent expires. Until the passage of the Hatch-Waxman Act, research to develop new drugs that involved use of a patented invention could not begin unless the researcher obtained a license under the patent, or purchased a commercially available patented compound, or until the relevant patent expired. A delay in starting research necessarily delayed the introduction of new and competitive drugs to the market. An objective of the Section 271(e)(1) exemption is to allow drug manufacturers to perform the clinical and preclinical work necessary to prepare and submit the IND and NDA for a drug without the risk of infringing others’ patents.

Understanding the boundaries of the infringement exemption under the Section 271(e)(1) exemption is of vital importance to concerns engaged in the development and evaluation of new uses for drugs and therapeutic biologicals. Absent such an understanding, companies risk liability for patent infringement and the loss of the very substantial capital investment and effort commonly expended in developing new uses for existing drugs and biologicals. Despite the critical significance of firmly understanding the scope of the exemption, the wording of the section is not precise. Moreover, the scope of the safe harbor has been largely unsettled since the Federal Circuit’s decision in the Integra/ Merck controversy, Integra Lifesciences I, Ltd. v. Merck KGaA, 331 F.3d 860 (Fed. Cir. 2003), in which the appeals court rather narrowly interpreted the exemption’s applicability to pre-clinical activities. The Federal Circuit framed the issue before it as whether the Section 271(e)(1) exemption extended as far back down the “chain of experimentation” as the “development and identification of new drugs that will, in turn, be subject to FDA approval.” It seems reasonable to assume that Congress did not intend Section 271(1)(e) as a blanket exemption of any and all pre-commercial activities related to a drug that is approved for marketing by FDA. The Federal Circuit, however, held that there must be a relatively direct relationship between the activity alleged to infringe and the submission of experimental data to FDA, and that the exemption did not include “general biomedical research to identify new pharmaceutical compounds.” The Federal Circuit stated that the exemption “does not globally embrace all experimental activity that at some point, however attenuated, may lead to an FDA approval process. The safe harbor does not reach any exploratory research that may rationally form a predicate for future FDA clinical tests.”

Thus, the Federal Circuit apparently considered activities intended to identify candidate drugs to be submitted for FDA approval as outside the safe harbor since such early stage activities are not, in the words of Section 271(e)(1), “solely for uses reasonably related to the development and submission of information” to FDA. Without such early stage activity, however, it may be impossible to identify candidate drugs warranting the further testing necessary to prepare and submit an IND to FDA. Against this backdrop, the pharmaceutical industry, the patent bar, and many others in the business and legal communities had eagerly awaited the United States Supreme Court’s decision reviewing the Federal Circuit’s Integra v. Merck decision. The Supreme Court broadly interpreted the “solely for uses reasonably related to” language and the scope of the safe harbor under Section 271(e)(1). Justice Scalia, writing for Court, acknowledged the inexact contours of the provision, but stated that “the statutory text makes clear that it provides a wide berth for the use of patented drugs in activities related to the federal
regulatory process,” and 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.” Slip Opinion at 8. The Court completely dismissed any notion that the phase of the research in which information is developed can be a basis for denial of the exemption. Slip Opinion at 9.

In addressing the Federal Circuit’s determination that the exemption does not globally embrace all experimental activity that might lead to an FDA submission, the Supreme Court agreed that “[b]asic scientific research on a particular compound, performed without the intent to develop a particular drug or a reasonable belief that the compound will cause the sort of physiological effect the researcher intends to induce, is surely not ‘reasonably related to the development and submission of information’ to the FDA.” Slip opinion at 12.

Here, the Supreme Court noted the concern expressed by the Federal Circuit that a limited construction of §271(e)(1) is necessary to preserve rights in patents to “research tools”, where the primary market, if not the only market, is often pharmaceutical companies and other researchers engaged in research where the information developed may be used in FDA submissions. Because the parties never argued, and the record did not show, that the Integra patents covered research tools, the Supreme Court declined to “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.” Slip Opinion at 12, n.7.

The Supreme Court departed from its agreement with the Federal Circuit’s concern for the global embrace of the research exemption, however, when it stated that “under certain circumstances” the exemption is sufficiently broad to protect the use of patented compounds in situations where there is “experimentation on drugs that are not ultimately submitted to the FDA.” Slip Opinion at 12.

Justice Scalia observed that the Federal Circuit’s narrow reading of the phrase “solely for uses reasonably related to clinical testing for FDA” to exclude from the exemption research used to identify the best candidate drugs disregards the reality that research is a trial and error process, particularly at the preclinical stage of drug approval. “Properly construed, §271(e)(1) leaves adequate space for experimentation and failure on the road to regulatory approval: At least where a drugmaker has a reasonable basis for believing that a patented compound may work, through a particular biological process, to produce a particular physiological effect, and uses the compound in research that, if successful, would be appropriate to include in a submission to the FDA, that use is ‘reasonably related’ to the ‘development and submission of information’ under the FDCA. Slip Opinion at 13-14.

While the Supreme Court’s decision clearly opens the exemption under §271(e)(1) to research developed during all stages of the regulatory process, the latter statement by the Court, as well as others throughout the opinion, suggest that questions such as the intent of the researcher, his or her belief that the patented invention may work, and whether or not the researcher had a particular biological process and a particular physiological effect in mind, although not stated in Section 271(e)(1), are relevant in determining whether or not the research qualifies for the exemption.

Christine R. Ethridge
cethridge@kln.com
412.355.8619

Mark R. Leslie
mleslie@kln.com
412.355.6271
Kirkpatrick & Lockhart Nicholson Graham LLP (K&LNG) has approximately 950 lawyers and represents entrepreneurs, growth and middle market, capital markets participants, companies and leading Fortune 100 and FTSE 100 global corporations nationally and internationally.

K&LNG is a combination of two limited liability partnerships, each named Kirkpatrick & Lockhart Nicholson Graham LLP, one qualified in Delaware, U.S.A. and practicing from offices in Boston, Dallas, Harrisburg, Los Angeles, Miami, Newark, New York, Palo Alto, Pittsburgh, San Francisco and Washington and one incorporated in England practicing from the London office.

If you have questions or would like more information about K&LNG’s Intellectual Property practice, please contact one of our lawyers listed below:

**Boston**
- Arthur Z. Bookstein 617.261.3153 abookstein@klng.com
- Michael H. Brodowski, Ph.D. 617.261.3113 mbrodowski@klng.com
- David J. Byer 617.261.3115 dbyer@klng.com
- Tara C. Clancy 617.261.3121 tclancy@klng.com
- John J. Cotter 617.261.3178 jcotter@klng.com
- Thomas F. Holt, Jr. 617.261.3165 tholt@klng.com
- Debra J. Peckham 617.261.3126 dpeckham@klng.com
- Jeffrey L. Snow 617.951.9233 jsnow@klng.com
- Thomas A. Turano 617.261.3148 tturano@klng.com
- Christine C. Vito Ph.D. 617.261.3150 cvito@klng.com

**Dallas**
- Julie E. Lennon 214.939.4920 jlennon@klng.com

**Harrisburg**
- Carlton O. Strauss 717.231.4503 cstrouss@klng.com

**London**
- Rachel Boothroyd 44.(0)20.7360.8255 rboothroyd@klng.com
- Dominic J. Bray 44.(0)20.7360.8191 dbray@klng.com

**Los Angeles**
- Paul W. Sweeney, Jr. 310.552.5055 psweeney@klng.com

**Miami**
- Anthony P. La Rocco 973.848.4014 alarocco@klng.com

**New York**
- Keith E. Danish 212.536.4063 kdanish@klng.com
- Anthony H. Handal 212.536.4870 ahandal@klng.com
- Mark I. Peroff 212.536.4865 mperoff@klng.com
- Darren W. Saunders 212.536.3952 dsanders@klng.com
- Whitney J. Smith 212.536.3930 wsmith@klng.com
- Kelly D. Talcott 212.536.4817 ktalcott@klng.com

**Palo Alto**
- Jon Michaelson 650.798.6704 jmichaelson@klng.com

**Pittsburgh**
- Terry Budd 412.355.8672 tbudd@klng.com
- David R. Cohen 412.355.8682 dcohen@klng.com
- George D. Dickos 412.355.6785 gdickos@klng.com
- Thomas J. Edgington 412.355.8303 tedgington@klng.com
- Christine R. Ethridge 412.355.8619 cethridge@klng.com
- James R. Kyper 412.355.6542 jkyper@klng.com
- Mark R. Leslie 412.355.6271 mleslie@klng.com
- Jerry S. McDevitt 412.355.8608 jmcdevitt@klng.com
- Patrick J. McElhinny 412.355.6334 pmcelhinny@klng.com
- Franklin B. Molin 412.355.6251 fmolin@klng.com
- Jonathan C. Parks 412.355.6288 j Parks@klng.com
- Charles M. Tea, III 412.355.6256 ctlea@klng.com
- Robert D. Yeager 412.355.8605 ryeager@klng.com

**San Francisco**
- Deborah Bailey-Wells 415.249.1065 dbaileywells@klng.com
- Kevin C. Trock 415.249.1021 ktrock@klng.com
- Kathryn M. Wheble 415.249.1045 kwheble@klng.com

**Washington**
- Stephen C. Glazer 202.778.9045 sglazier@klng.com

This publication/newsletter is for informational purposes and does not contain or convey legal advice. The information herein should not be used or relied upon in regard to any particular facts or circumstances without first consulting a lawyer.

© 2005 KIRKPATRICK & LOCKHART NICHOLSON GRAHAM LLP. ALL RIGHTS RESERVED.