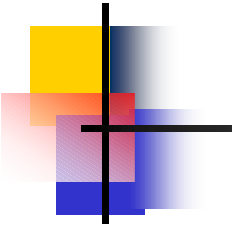




**THE HATCH-WAXMAN ACT
AND PATENTS THAT COVER RESEARCH
AND SCREENING FOR DRUGS**

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THE PHARMACEUTICAL INDUSTRY BEFORE 1984 – PART I

- Research-based companies complained that they *de facto* received shorter patent term than mandated by Congress because of delay in obtaining FDA approval.
- Generic companies complained that the research-based companies *de facto* received longer patent term than mandated by Congress because:
 1. uncertain whether conducting clinical trial constituted patent infringement; and
 2. had to repeat complete clinical trial, i.e. safety and efficacy.



THE PHARMACEUTICAL INDUSTRY BEFORE 1984 – PART II

- Significant enmity between the research-based and generic industries.
- Each had a powerful lobby.
- Congress indicated willingness to pass a bill as long as both industries approved.



GENERAL PATENT INFRINGEMENT

- 35 U.S.C. 271(a)

Except as otherwise provided in this title, whoever without authority makes, uses, offers to sell or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefor, infringes the patent. (Emphasis added)



COURT-MADE EXPERIMENTAL USE EXCEPTION TO PATENT INFRINGEMENT

- Justice Story in *Whittemore v. Cutter*, 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813)

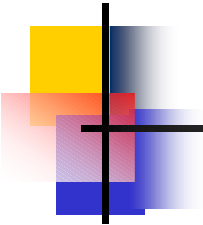
“[I]t could never have been the intention of the legislature to punish a man (or woman), who constructed such a machine merely for philosophical experiments, or for the purpose of ascertaining the sufficiency of the machine to produce its described effects.”



LIMITATION OF EXPERIMENTAL USE EXCEPTION

- *Roche Products v. Bolar Pharmaceuticals*, 733 F.2d 858, 863 (Fed. Cir. 1984)

“Bolar’s intended ‘experimental’ use is solely for business reasons and not for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry. Bolar’s intended use of (Roche’s patented drug) to derive FDA-required test data is thus an infringement of (Roche’s) patent.”



GRAND COMPROMISE - THE PATENT TERM EXTENSION AND DRUG PRICE COMPETITION ACT OF 1984 (HATCH-WAXMAN ACT) - PART I

- Research-based pharmaceutical companies wanted and got:
 - automatic five years of exclusivity for a new drug irrespective of patent protection, 21 U.S.C. §355(c)(3)(D)(ii), and
 - patent term extension up to five years to compensate for term lost during clinical trials, 35 U.S.C. 156.



GRAND COMPROMISE - THE HATCH-WAXMAN ACT - PART II

- Generic companies wanted and got:
 - exemption from infringement during clinical trials.
 - Safe Harbor Provision.
 - Congress overruled *Roche v. Bolar*.
 - the Abbreviated New Drug Application (ANDA).



THE SAFE HARBOR PROVISION OF THE HATCH-WAXMAN ACT OF 1984

- 35 U.S.C. §271 (e)(1)

It shall not be an act of infringement to make, use, 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.
(Emphasis added)



EXAMPLE OF CONFUSION

- Generic company uses patented drug to conduct ANDA, and:
 - Submits data to FDA - **Exempt!**
 - Disseminates data at scientific conference to recruit investigators - **Loss of Exemption?**
 - Are activities “solely for uses reasonably related” to developing information for submission to FDA?
 - Possible reasons to maintain exemption:
 1. Reasonably related.
 2. Non-infringing activity.



NOT “AN ELEGANT PIECE OF STATUTORY DRAFTSMANSHIP”

- Justice Scalia says of §271 (e)(1) :

“No interpretation we have been able to imagine can transform §271 (e)(1) into an elegant piece of statutory draftsmanship.”

Eli Lilly and Company v. Medtronic, Inc., 496 U.S. 661; 110 S. Ct. 2683; 110 L. Ed. 2d 605; 1990 U.S. LEXIS 3184; 58 U.S.L.W. 4838; 15 U.S.P.Q.2d 1121 (1990)



ISSUE

- When are activities “solely for uses reasonably related” to conducting clinical trials?



EARLY CASES RELATED TO PRODUCTS ALREADY IN CLINICAL TRIALS

- *Intermedics, Inc. v. Ventritex, Inc.*, 775 F. Supp. 1269, 1277 (N.D. Cal. 1991), aff'd without opinion, 991 F.2d 808 (Fed. Cir. 1993)
- *Elan Transdermal Ltd. v. Cygnus Therapeutics Systems*, 24 U.S.P.Q.2d 1926, 1931-1932 (N.D. Cal. 1992)
- *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019, 1028 (Fed. Cir. 1997)
- *Nexell Therapeutics, Inc. v. AmCell Corp.*, 199 F. Supp. 2d 197, 199 (D. Del., 2002)
- *Telectronics Pacing Sys. Inc. v. Ventritex, Inc.*, 982 F.2d 1520, 1525 (Fed. Cir. 1992)



TYPES OF FEDERAL CIRCUIT DECISIONS

- panel v. *en banc* decisions
- precedent v. non-precedent decisions



LIBERAL STANDARD

“Would it have been **reasonable, objectively**, for a party in (defendant’s) situation to believe that there was **a decent prospect** that the ‘use’ in question would contribute **(relatively directly)** to the generation of **kinds of information** that was **likely to be relevant** in the processes by which the FDA would decide whether to approve the product?” (Emphasis added)



PERMITTED ACTIVITIES FOR PRODUCTS ALREADY IN CLINICAL TRIALS

- Demonstration of medical device and use of data at medical conferences in order to recruit clinical investigators.
- Sales to hospitals for use in clinical trials.
- Demonstration of medical device and use of data at medical conferences in order to raise money for clinical trials.
- Using data to obtain approval outside the United States (“ . . . solely for uses reasonably related to the development and submission of information . . . ” inside the United States.



LIBERAL STANDARD ALSO APPLIED TO ACTIVITIES INVOLVING PRODUCTS NOT IN CLINICAL TRIALS

- Examples of activities involving products not yet in clinical trials:
 - Making compounds to screen.
 - Screening patented drug candidates.
 - Other pre-clinical research.



Chartex Int'l PLC v. M.D. Pers. Prod. Corp. et al. - PART I

- Pre-clinical activities held to be non-infringing:
 - Displaying patented female condoms at trade shows.
 - Conducting consumer studies to evaluate consumer acceptance.

5 F.3d 1505; 1993 (Fed. Cir. 1993)



Chartex Int'l PLC v. M.D. Pers. Prod. Corp. et al. - PART II

- Pre-clinical activity held to be reasonably related to obtaining information for FDA approval:
 - Use of the condom experimentally by an employee “to determine its suitability for the FDA studies.”
- Unpublished opinion.

5 F.3d 1505; 1993 (Fed. Cir. 1993)



Bristol-Myers Squibb Company v. Rhone Poulenc Rorer, Inc.

- Using claimed taxol intermediates to run “hundreds of experiments for purposes of possibly identifying a drug candidate.” *Id.* at 14.
- Excused under the safe harbor provision.
- Led to uncertainty of the value of drug screening patents.

2001 U.S. Dist. LEXIS 19361 (S.D.N.Y. 2001)



CONSENSUS BEFORE JUNE 6, 2003

- PART I

- *Nexell Therapeutics, Inc. v. AmCell Corp.*, 199 F. Supp. 2d 197, 199 (D. Del., 2002)

Unless the court is confronted with the extreme case in which . . . it is clear that certain otherwise infringing activities are outside the FDA approval process . . . , the court will not find that accused activities that a defendant objectively believes could generate information that is likely to be relevant to the FDA approval process are not “reasonably related” to obtaining FDA approval. (Emphasis added)



CONSENSUS BEFORE JUNE 6, 2003

- PART II

- Jones, Philip B.C., *Food and Drug Law Journal* 57, 475, 489 (2002)

“It is likely that courts will maintain the expansive depth and breadth of the Hatch-Waxman Act’s safe harbor in the foreseeable future.”



THE FEDERAL CIRCUIT SPEAKS

- *Integra Lifesciences v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003) Facts:

Integra owned four patents related to certain peptides having the sequence RGD. The peptides showed potential as anti-angiogenesis compounds.

Scripps (on behalf of Merck) conducted experiments “to evaluate the specificity, efficacy, and toxicity of (three RGD peptides) for various diseases, to explain the mechanism by which these drug candidates work, and to determine which candidates were effective and safe enough to warrant testing in humans.”

The research led to a lead candidate.

Integra at 863.



AT THE DISTRICT COURT (S.D. California 1999)

- At trial, the district court held that Merck infringed the Integra patents, and that the infringement was not exempt under the safe harbor provision.

Integra at 863.



THE ISSUE ON APPEAL

- On appeal, the Federal Circuit stated the issue as:
 - . . . whether the §271(e)(1) Safe Harbor reaches back down the chain of experimentation to embrace development and identification of new drugs that will, in turn, be subject to FDA approval. (Emphasis added)

Integra at 865.



THE CHAIN OF EXPERIMENTATION

- In *Bristol-Myers Squibb*, BMS used the patented intermediates to discover possible drug candidates.
- In *Integra*, Scripps (on behalf of Merck) made three patented peptides as possible candidates, and determined which warranted clinical testing.



HOLDING

- The Federal Circuit in *Integra* held:

The “exemption of §271(e)(1) did not embrace the infringing activity.”



LEGISLATIVE HISTORY

The Federal Circuit began its analysis by reviewing the legislative history of the Hatch-Waxman Act.

Safe harbor covers only:

- “. . . a limited amount of testing so that generic manufacturers can establish the bioequivalency of a generic substitute.”
- “. . . all that the generic (company) can do is test the drug for purposes of submitting data to the FDA for approval. Thus, the nature of the interference (to the patent owner) is *de minimus*.”

Integra at 865.



THE SAFE HARBOR IS CLOSED TO ALL BUT A FEW BOATS IN A STORM - PART I

- The Federal Circuit in *Integra* emphasized how narrowly it viewed the safe harbor provision by stating that it covers only:
 - . . . those pre-expiration activities of a drug already on the market “reasonably related” to acquiring FDA approval. (Emphasis added)



THE SAFE HARBOR IS CLOSED TO ALL BUT A FEW BOATS IN A STORM - PART II

- “The safe harbor does not reach any exploratory research that may rationally form a predicate for future FDA clinical tests.”

Integra at 867.



RESEARCH TOOLS

- The Federal Circuit entered the heated debate regarding research tool patents decisively on the side of such patents:
 - . . . expansion of §271(e)(1) to include the (defendant's) activities would effectively vitiate the exclusive rights of patentees owning biotechnology tool patents. After all, patented tools often facilitate general research to identify candidate drugs, as well as downstream safety-related experiments on those new drugs ...



SUMMARY OF *Integra*

- Strongly pro-patent.
- Safe harbor exemption from infringement narrowly protects only ANDA-related activities of generic companies.
- Using patented research and screening methods to discover new drugs is NOT exempt.



THE FEDERAL CIRCUIT WAS A LITTLE DEFENSIVE IN *Integra*

- The Federal Circuit apparently acknowledged the inconsistency of its decision with previous decisions by stating:

This court has not considered the question arising in this case, namely, whether pre-clinical research is exempt from liability for infringement of *Integra's* patents under §271(e)(1).

Integra at 865.



MAYBE THE FEDERAL CIRCUIT HAD REASON TO BE A LITTLE DEFENSIVE - PART I

- Judge Rader, who wrote the *Integra* decision, also wrote the *Chartex* decision.



MAYBE THE FEDERAL CIRCUIT HAD REASON TO BE A LITTLE DEFENSIVE - PART II

- *Chartex*: The safe harbor excused an employee who “...used the (patented) prototypes experimentally to determine if the device was ready for FDA feasibility studies.”
- *Integra*: “The safe harbor does not reach any exploratory research that may rationally form a predicate for future FDA clinical tests.”



A NOTE OF CAUTION - PART I

- The *Integra* decision was decided by a panel of judges. A request for reconsideration and suggestion for rehearing *en banc* was filed by Merck and is still pending.
- How the scope of §271(e)(1) is interpreted by a different panel or *en banc* remains uncertain. There have been issues in the past that were decided differently by different panels.



A NOTE OF CAUTION - PART II

- Is subject matter disclosed but not claimed in a patent dedicated to the public and, therefore, outside the doctrine of equivalents?
 - *Maxwell v. J. Baker, Inc.* 86 F.3d 1098, 39 U.S.P.Q.2d 1001 (Fed. Cir. 1996) - **Yes**
 - *YBM Magnex, Inc. v. Int'l Trade Comm'n*, 145 F.3d 1317, 46 U.S.P.Q.2d 1843 (Fed. Cir. 1998) - **No**
 - *Johnson & Johnston Associates v. R.E. Service Co., Inc. et al.*, 285 F.3d 1046 (Fed. Cir. 2002) (*en banc*) - **Yes**



A NOTE OF CAUTION - PART III

- Are product-by-process claims limited to products produced by the claimed process?
 - *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 18 U.S.P.Q.2d 1001 (Fed. Cir. 1991) - **No**
 - *Atlantic Thermoplastics Co., v. Faytex Corporation*, 970 F.2d 834, 23 U.S.P.Q.2d 1481 (Fed. Cir. 1992) - **Yes**



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