

# Seed<sup>IP</sup>

## Recent Federal Circuit and Supreme Court Cases Affecting Biotech Companies

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## Pfizer v. Apotex, Federal Circuit, 2007

- U.S. patent 4,572,909 to Pfizer claims amlodipine (Norvasc®) and pharmaceutically acceptable acid addition salts. Maleate salt identified as preferred.
- Pfizer later determines besylate salt is superior and is granted U.S. patent 4,879,303 claiming besylate salt
- Apotex filed ANDA to sell generic version of amlodipine besylate claiming '303 patent invalid for obviousness and other grounds

## Apotex continued

Is making besylate salt of known compound obvious?

- Court considered four factors in finding obviousness:
  - Motivation to combine prior art references
  - Reasonable expectation of success
  - Obvious to try
  - Secondary considerations

## Apotex continued

- Motivation to combine prior art references:
  - Need not be found explicitly in prior art reference, but can be found from many sources including common knowledge, prior art as a whole or the nature of the problem
  - Because maleate was unstable, one would be motivated to try any one of 53 approved salts to solve problem

**Held:** Skilled artisan would have been motivated to combine prior art references

## Apotex continued

- Reasonable expectation of success:
  - Obviousness cannot be avoided by simply showing some degree of unpredictability if there is a reasonable probability of success
  - Pfizer's own prior art contained strong suggestion that all pharmaceutically acceptable anions would work for the intended purpose

**Held:** Skilled artisan would have had reasonable expectation of success

## Apotex continued

- Obvious to try:
  - Fact dependent inquiry
  - Numerous publications taught various besylate salts
  - Routine in art to make and test various salts
  - Discovery of optimum value of a variable in a known process is usually obvious

**Held:** Would have been obvious to try to optimize acid addition salt formulation

## Apotex continued

- Secondary considerations:
  - Is Pfizer's showing of superior results (stability, stickiness, etc.) enough to rebut prime facie case of obviousness?
  - Superior property must be unexpected
    - One skilled in the art would expect different anions to impart different properties – some inferior and some superior

**Held:** Pfizer's superior results are not unexpected such that a prime facie case of obviousness is rebutted

KSR v. Teleflex,  
Supreme Court, 2007

- Teleflex owns rights to Engelgau patent claiming position-adjustable pedal assembly with an electronic pedal position sensor attached to a fixed pivot point
- KSR owns patent to adjustable pedal system with cable-actuated throttle – sought to add sensor to design
- Teleflex sued for infringement and KSR countered alleging Teleflex patent invalid for obviousness

## KSR Continued

Is it obvious to combine Asano's pedal with a pivot-mounted position sensor?

- **Prior art:**
  - Asano patent discloses adjustable pedal with fixed pivot point
  - '936 patent discloses pedal with electronic sensor on a pivot point
  - Smith patent discloses mounting sensor on fixed part of pedal assembly
  - Rixon patent discloses attaching sensor to pedal foot pad of adjustable pedal assembly

## KSR Continued

- Common sense teaches that familiar items may have obvious uses beyond their primary purpose
  - Asano's primary purpose was a pedal that ensures constant force, but it disclosed adjustable pedal with fixed pivot and other art taught fixed pivot point was ideal sensor mount
- When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp

## KSR Continued

- Rigid application of teaching-suggestion-motivation (TSM) test rejected
  - Supreme court mandates “Expansive and flexible” approach, one that allows for the common sense and ordinary creativity of those of ordinary skill in the art
  - TSM test is not necessarily inconsistent with proper application of 35 U.S.C. § 103

**Held:** Claimed invention obvious in light of Asano’s patent, marketplace demand for converting mechanical pedals to electronic and prior art teachings for how to achieve that

## KSR Continued

- Directions to lower courts:
  - Determine whether there was apparent reason to combine known elements
  - Ask whether improvement is more than predictable use of prior art elements according to their established functions
  - Need not seek out precise teachings but can take into account inferences and creative steps skilled artisan would employ
  - TSM test is helpful insight but analysis cannot be confined by a formalistic conception

## KSR Continued

- How does the USPTO handle the KSR decision?
- May 3, 2007 memo:
  - “Therefore, in formulating a rejection under 35 U.S.C. 103(a) based upon a combination of prior art elements, it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed.”

Ex Parte Kubin (Immunex/Amgen)  
BPAI, 2007

## Obviousness in biotech patent post KSR

- Invention directed to nucleic acid sequence encoding NAIL protein for modulation of NK cells (immune response)
- Prior art teaches p38 (NAIL) and how to isolate p38 cDNA
- Different reference teaches using mAb C1.7 for isolation of p38 cDNA

## Ex Parte Kubin continued

Is claimed nucleotide obvious based on disclosure of p38 and teachings how to isolate its cDNA?

- Under KSR, “obvious to try” standard is appropriate
- Problem was to isolate NAIL c DNA and there were a limited number of methodologies available
- Skilled artisan had reason to try the methodologies with reasonable expectation of success
- BPAI would not apply TSM test
- **Held:** invention obvious

Takeda Chem. V. Alphapharm  
Federal Circuit, 2007

Obviousness in chemical patent post KSR

- Takeda owns patent to \$1.7 billion diabetes drug - ACTOS®
- Generic drug makers, Alphapharm and Genpharm, file ANDA and allege Takeda’s patent was obvious in light of KSR decision
- Takeda’s compound has 5-ethylpyridyl moiety, prior art compound has 6-methylpyridyl moiety

## Takeda Chem. continued

Is modification of known chemical structure obvious?

Graham v. John Deere factors still control:

1. Scope and content of prior art
2. Difference between prior art and the claims
3. Level of ordinary skill in the pertinent art
4. Objective evidence of nonobviousness

## Takeda Chem. continued

- In chemical cases normally a prime facie case of obviousness is based on structural similarity but
  - A showing that the prior art suggested making the specific modification is also required
- Court found no motivation in prior art and that prior art actually taught away from Takeda's compound
- **Held:** Takeda's compound not obvious

## Takeda Chem. continued

- Court emphasized that decision is in line with KSR because KSR acknowledged that it is still important to identify a reason that would prompt modifying prior art
- Court concluded that in cases with new chemical compounds it is still necessary to identify reason why chemist would be motivated to modify a known compound
- Gives some relief that not everything is obvious after KSR and Apotex

In Re Seagate  
Federal Circuit, August 20, 2007

- Convolve Inc. filed complaint alleging Seagate infringed three of their patents
- Prior to lawsuit, Seagate obtained opinion of counsel which concluded that Seagate's products did not infringe two of the patents – additional opinion on third patent obtained after lawsuit filed
- Seagate disclosed opinions and made attorney available for deposition
- Seagate's opinion counsel and trial counsel operated independently

## In Re Seagate continued

- Federal circuit addressed three issues:
  - When may a court award enhanced damages for patent infringement?
  - What is the scope of the waiver triggered by reliance on the advice of counsel as a defense to an allegation of willful infringement?
  - Does the waiver extend to trial counsel's work product?

## In Re Seagate continued

- When may a court award enhanced damages for patent infringement?
  - Court expressly overruled *Underwater Devices* affirmative duty of due care standard
  - Proving willful infringement requires at least showing of objective recklessness – 2 part test
    - Patentee must show by clear and convincing evidence that infringer acted despite objectively high likelihood of infringing
    - Patentee must show that risk was known or should have been known
  - No affirmative obligation to obtain opinion of counsel

## In Re Seagate continued

- What is the scope of the waiver triggered by reliance on the advice of counsel as a defense to an allegation of willful infringement?
  - Different functions of trial and opinion counsel advice against extending waiver
  - Disclosing opinions of patent opinion counsel does not result in waiver of attorney-client privilege for communications with trial counsel

## In Re Seagate continued

- Does the waiver extend to trial counsel's work product?
  - Relying on opinion counsel's work product does not waive work product immunity with respect to trial counsel
  - General principles of discovery of work product remain in force
  - Exception if patentee or counsel engages in 'chicanery'

## In Re Seagate continued

### Unresolved questions:

- ☞ What is patentee's burden of proof for second part of test?
- ☞ What sort of evidence can be used to show recklessness?
- ☞ Is bifurcation of trial on willfulness issues appropriate?
- ☞ What constitutes 'chicanery'?

## Ebay v. MercExchange U.S. Supreme Court, 2006

- MercExchange owns business method patent for on-line sales.
- Ebay is on-line auction company sued by MercExchange for patent infringement.
- District Court held MercExchange's patent valid and infringed. Awarded damages but denied permanent injunction.

## MercExchange continued

- Federal Circuit reversed the denial of permanent injunction, applying general rule that “courts will issue permanent injunctions against patent infringement absent exceptional circumstances.”
- Supreme Court held permanent injunctions are remedy based on equitable principles and evaluated under four-factor test. No “general rule” for automatic injunction in patent cases.

## Permanent Injunctions

- Not automatically granted in patent cases.
- Must follow traditional four-part test for determining if equitable remedy is appropriate.

## MercExchange continued

### Four-Factor Test

- Patent owner seeking injunction must show:
  - I. Patent owner will suffer irreparable injury.
  - II. Remedies available at law (money damages) are inadequate.
  - III. Equitable remedies are warranted (balance of hardships).
  - IV. Public interest would not be disserved by granting injunction.

## Unanswered Questions

- What is “irreparable injury”?
- What impact on test is infringer’s willingness to license a patent if it is not sufficient to establish patent holder would not suffer irreparable harm?
- If injunction is denied, how are damages calculated and is ongoing infringement willful?

## Interpreting 35 U.S.C. § 271(e)(1)

Merck v. Integra,  
U.S. Supreme Court, 2005

## 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 (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) 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.”

## Merck v. Integra Lifesciences, Inc., U.S. Supreme Court, 2005

- Merck contracted with Scripps to do research for FDA drug approval of RGD peptides.
- Research led to discovery of a specific RGD-peptide that inhibits angiogenesis (blood vessel growth).
- Integra had patents for the RGD-peptides and for certain screening methods.

## Merck v. Integra (continued)

- Integra offered Merck licenses, but Merck declined.
- Integra sued Merck and Scripps for patent infringement.
- Merck asserted its research qualified under the “safe harbor” of 35 U.S.C. § 217(e)(1).
- District court, following jury trial, ruled that Merck’s activities did not fall under § 271(e)(1), and Merck infringed Integra’s patent.

## Merck v. Integra (continued)

- Federal Circuit affirmed the district court's ruling of patent infringement.
- Supreme Court vacated and remanded the decision, finding Merck's activities fell within the parameters of 35 U.S.C. § 271 (e)(1).

## Merck v. Integra (continued)

- Is Merck's screening and pre-clinical research exempt from infringement under 35 U.S.C. § 271(e)(1)?
- Case remanded for analysis of evidence under this standard.
- Legal Conclusion: The § 271(e)(1) exemption "extends to all uses of patented inventions that are reasonably related to the development and submission of any information under FDCA."

## Merck v. Integra (continued)

- “Reasonably related” defined:  
“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.”

## Merck v. Integra (continued)

- Data is exempt if “reasonably related to development and submission of information to the FDA”—even if not actually submitted.
  - Pre-Clinical data (in vitro or in vivo)
  - Clinical data
  - Pharmacological, toxicological, pharmacokinetic, and biological quality data
  - Safety and efficacy drug research

## Merck v. Integra (continued)

## Limitation to § 271(e)(1):

Basic scientific research done without intent to develop a drug or without reasonable belief the compound will induce the desired physiological effect is not exempt from infringement.

## Merck v. Integra (continued)

- Footnote 7: Supreme Court explicitly declines to comment on any effect § 271(e)(1) may have on the use of patented research tools.
- Supreme Court made strong statements regarding compositions and specifically those used as controls.

## Bottom Line for § 271(e)(1) exemption

- Research done with the intent to develop a particular drug is exempt.
- Research done with a “reasonable belief” that a particular compound will induce an intended physiological effect is exempt.
- Basic scientific research is not exempt.
- No conclusive decision as to patented research tools.

## Practice Tip

- Any R & D done with patented compounds must have “intent” to submit to FDA, or may not be exempt from infringement.
- Stay tuned...case was remanded for further analysis of evidence.
- Research Tool Patents → still up in the air...where do we go from here?

## MedImmune v. Genentech, U.S. Supreme Court, 2006

- Genentech owns patents for chimeric antibodies and coexpression of immunoglobulin chains in recombinant host cells ('Cabilly II patent').
- MedImmune manufactures Synagis, a respiratory drug.
- MedImmune is a licensee of Genentech's Cabilly II patent, and filed a declaratory judgment action challenging the patent's validity and enforceability.

## MedImmune continued

- MedImmune claims Synagis does not infringe the Cabilly II patent, and the Cabilly II patent is invalid and unenforceable.
- District Court dismissed the case for lacking subject-matter jurisdiction, under *Lear v. Adkins* and *Gen-Probe* cases.
  - *Lear* and *Gen-Probe* cases held patent licensee in good standing cannot establish an Article III case or controversy for validity, enforceability or scope of licensed patent.

## MedImmune continued

- Federal Circuit affirmed.
- U.S. Supreme Court reversed.
- Holding: a case or controversy exists where the facts show a substantial controversy “between parties having adverse legal interests, of sufficient immediacy and reality to warrant” relief.
- Parallel government threat of imminent harm vs. private party threat.

## MedImmune continued

- Parties did not settle dispute by entering into license agreement.
- Licensee’s option of ceasing royalty payments would have risked award of actual and treble damages for willful infringement in later patent suit.
- Cabilly II patent is invalid, unenforceable or not infringed by MedImmune.
- Remanded to Federal Circuit.

## Unanswered Questions

- Which licenses are “settlements” to patent disputes?
- When does a “genuine threat of enforcement” exist?
- Can a licensee protect itself from such challenges by additional terms in the underlying license agreement? (e.g., unsuccessful challenge doubles or triples royalties or milestone payments and adds attorney fees)

THANK YOU FOR YOUR ATTENTION

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