

# Pharmaceuticals and Biotechnology: PTO's 2010 Obviousness Guidelines

presentation by

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of

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to

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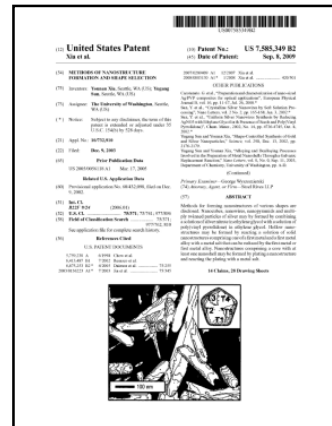
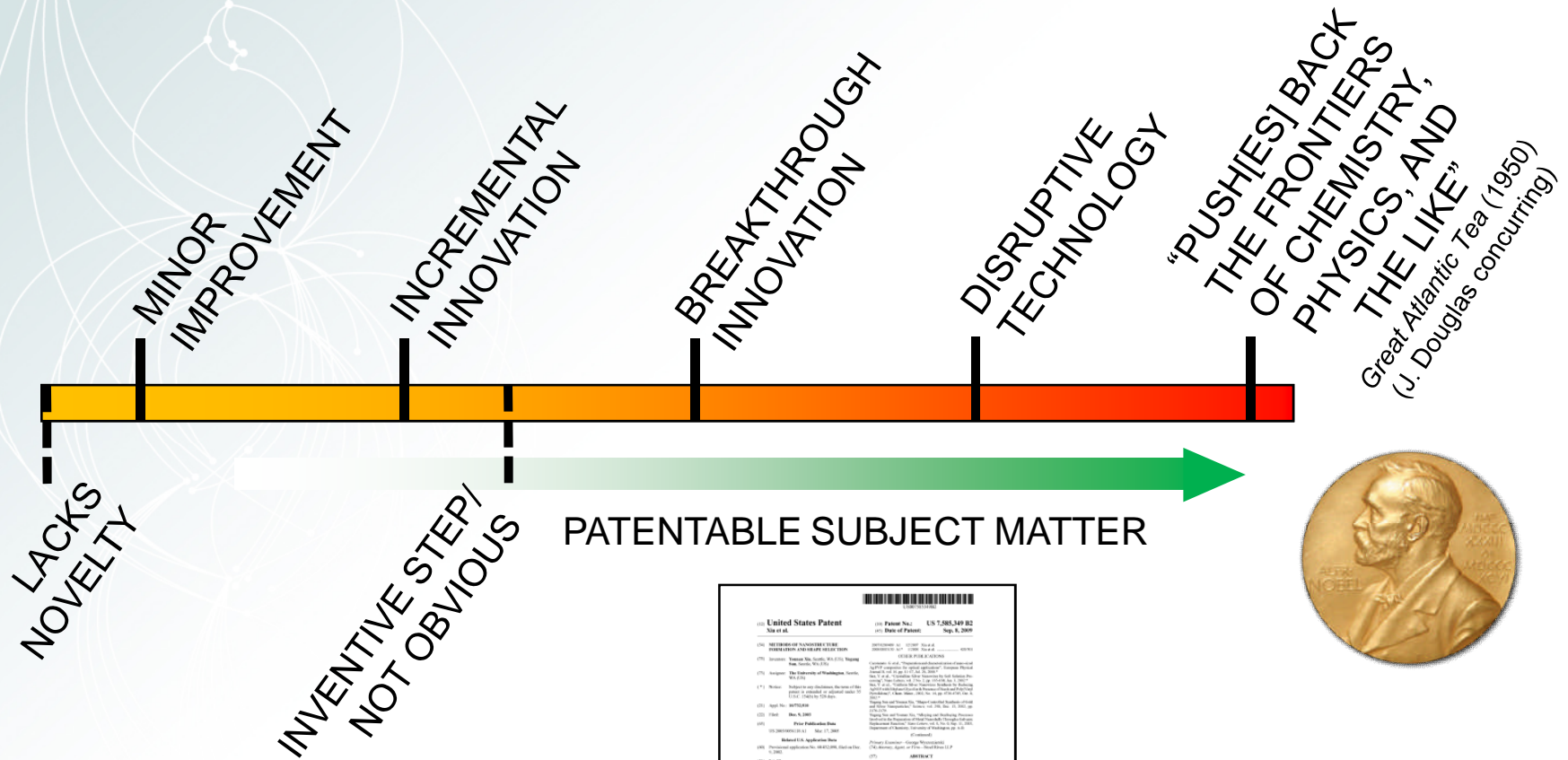


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# Innovation Continuum



## §103 in the 1952 Patent Act

- A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.



# Graham v. John Deere Co. (1966)

- In Graham v. John Deere, a test was formulated for the issue of patentability under §103. Under §103,
  - (1) “the scope and content of the prior art are to be determined;
  - (2) “differences between the prior art and the claims at issue are to be ascertained;” and
  - (3) “the level of ordinary skill in the pertinent art resolved.”
  - And . . . “[s]uch secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., ... may have relevancy.”



# Federal Circuit's Obviousness Jurisprudence

- The Court of Appeals for the Federal Circuit (FC) was created in 1982 to achieve doctrinal stability in patent law.
- The FC developed the teaching-suggestion-motivation (TSM) test:
  - when prior art references contain different elements of a claimed invention, the references can be combined to find obviousness of the claimed invention only when there is some teaching, suggestion or motivation to combine the prior art references.



# §103 and the TSM test

- *In re Dembiczak* (Fed. Cir. 1999)
  - “Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement of a showing of the teaching or motivation to combine prior art references.”



PRIOR ART



“INVENTION”

- Obviousness cases are factually dependent, so some results may be outlying and easily caricatured.
  - “As a trip to the checkout counter at most grocery stores will reveal, the selection of ‘paper or plastic’ is a quite routine set of alternative materials for bagging purposes.”  
Roger E. Schechter et al., *Principles of Patent Law* 161 (2004).



# §103 and the TSM test

- §103 states that the analysis of obviousness is based on whether “the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.”
- Critics asserted that the emphasis on prior art as opposed to the analysis by a person having ordinary skill in the art (PHOSITA) relegated the PHOSITA to at best a librarian and at worst an automaton. By elevating the art above a creative PHOSITA, the standard for obviousness was too low and approached novelty.



# Oral Arguments at the Supreme Court in KSR v. Teleflex (2007)

- U.S. Supreme Court last addressed obviousness in 1976.
- Scalia: “I agree with the Chief Justice. It is misleading to say that the whole world is embraced within these three nouns, teaching, suggestion, or motivation, and then you define teaching, suggestion, or motivation to mean anything that renders it nonobvious. This is gobbledygook. It really is, it’s irrational.



# Obviousness standards in the U.S. - “Goobledygook” evolves

- The U.S. Supreme Court held in *KSR v. Teleflex* that the TSM test was applied by the FC in a narrow, rigid manner that is inconsistent with § 103 and *Graham v. John Deere*.
- PTO provided 2007 KSR Guidelines, based on rationales for finding obviousness detailed in *KSR*, which were subsequently incorporated into the Manual of Patent Examining Procedure (MPEP) at § 2141 and § 2143
- On September 1, 2010, the PTO provided “Examination Guidelines Update: Developments in the Obviousness Inquiry after *KSR v. Teleflex*”



# MPEP §2143

- “KSR identified a number of rationales to support a conclusion of obviousness which are consistent with the proper “functional approach” to the determination of obviousness as laid down in *Graham*.”
- These rationales are detailed in Rationales A-G of §2143 which is titled: “**Examples of Basic Requirements of a *Prima Facie* Case of Obviousness.**”



# PTO's Obviousness Rationales - § 2143

- A. Combining prior art elements according to known methods to yield **predictable** results.
- B. Simple substitution of one known element for another to obtain **predictable** results.
- C. Use of known technique to improve similar devices (methods, or products) in same way and the result would have been **predictable**.
- D. Applying a known technique to a known device (method, or product) ready for improvement to yield **predictable** results.
- E. “Obvious to try”—choosing from a finite number of identified, **predictable** solutions, with a reasonable expectation of success.
- F. Known work in one field may prompt variations of it for use in same field or different one based on design incentives or market forces if the variations are **predictable**.
- G. The teaching-suggestion-motivation (TSM) test.
- H. Anything else that can be used to prove obviousness.



# PTO's Obviousness Rationales - § 2143

## 2010 KSR Guidelines Update:

Focus on additional guidance in view of decisions by the Federal Circuit since the KSR decision, including “teaching points”, in 3 of the rationales;

- A. Combining prior art elements according to known methods to yield **predictable** results (i.e.  $A_{\text{known}} + B_{\text{known}} \Rightarrow A-B$ )
- B. Simple substitution of one known element for another to obtain **predictable** results (i.e.  $A_{\text{known}} \Rightarrow A'$ )
- E. “Obvious to try”—choosing from a finite number of identified, **predictable** solutions, with a reasonable expectation of success

(i.e. **A - Z**  $\Rightarrow$  obvious to try; **A -  $\infty$**   $\Rightarrow$  invention)



# MPEP §2143, Rationale A

- Eight cases are profiled in Rationale A of the MPEP and the 2010 KSR Guideline Update
  - Anderson's-Black Rock v. Pavement Salvage Co., 396 U.S. 57 (1969)
  - Ruiz v. AB Chance, 357 F.3d 1270 (Fed. Cir. 2004)
  - In re Omeprazole Patent Litigation (Fed. Cir. 2008)
  - Crocs Inc v US ITC (Fed. Cir. 2010)
  - Sundance v DeMonte Fabricating (Fed. Cir. 2008)
  - Ecolab v FMC Corp (Fed. Cir. 2009)
  - Wyers v Master Lock (Fed. Cir. 2010)
  - DePuy Spine v Metronic Safamor Danek (Fed. Cir. 2009)

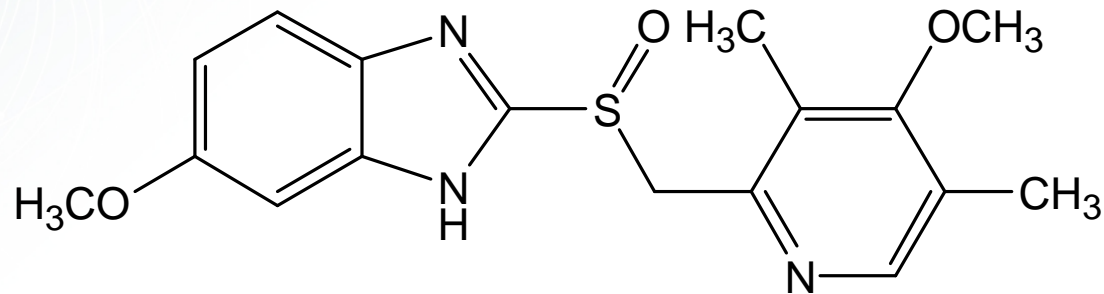


# In re Omeprazole

[AstraZeneca v. Apotex]

536 F.3d 1361 (Fed. Circ. August 20, 2008)

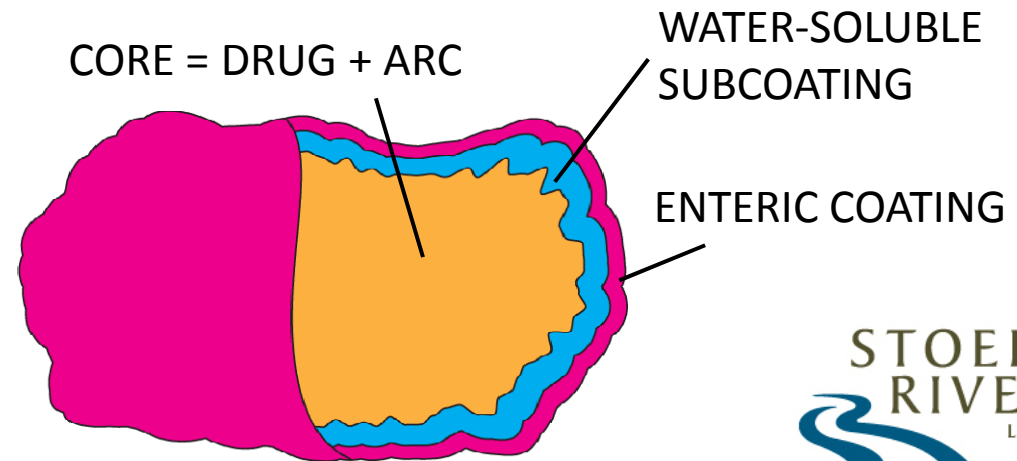
- omeprazole (Prilosec); PPI for ulcers, GERD



omeprazole

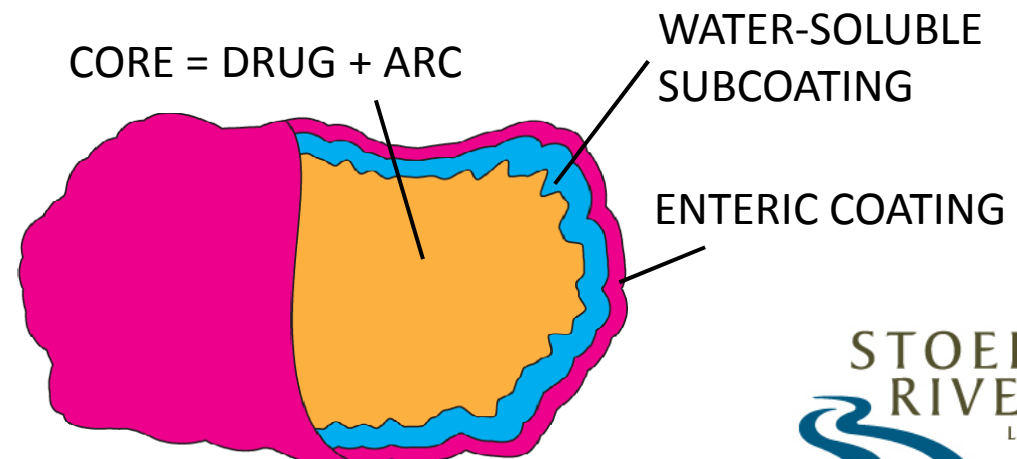
# In re Omeprazole

- AstraZeneca found that alkaline reacting compound (ARC) addition to drug core helped stabilize drug in storage, and that an enteric coating was needed to keep drug from decomposing in the stomach, but normal enteric coatings were known to dissolve the ARC
- AZ determined that a water-soluble subcoating would keep ARC intact but allow drug release in small intestine



# In re Omeprazole

- no prior art showed a negative interaction between ARC and enteric coatings or discussed subcoatings, thus no motivation to introduce a subcoating; not obvious
- even if there were motivation, a water-soluble subcoating would not be obvious to try



# In re Omeprazole

- 2010 KSR Guidelines “teaching point”

“Even where a general method that could have been applied to make the claimed product was known and within the level of skill of the ordinary artisan, the claim may nevertheless be nonobvious if the problem which had suggested use of the method had been previously unknown.”



# Practice tips for overcoming rejection based on MPEP §2143 Rationale A:

A. Combining prior art elements according to known methods to yield **predictable** results.

(i.e.  $A_{\text{known}} + B_{\text{known}} \Rightarrow A-B$ )

To address an obviousness rejection:

- argue that the results were not predictable
- argue that the problem was unknown
- argue that an unknown method was used to solve the problem



# MPEP §2143, Rationale B

- Eleven cases are profiled in Rationale B of the MPEP and the 2010 KSR Guidelines Update

- In re Fout, 675 F.2d 297 (CCPA 1982)
- In re O'Farrell, 853 F.2d 894 (Fed. Cir. 1988)
- Ruiz v. AB Chance, 357 F.3d 1270 (Fed. Cir. 2004)
- Ex parte Smith, 83 USPQ2d 1509 (BPAI 2007)
- In re ICON Health & Fitness (Fed. Cir. 2007)
- Agrizap v Woodstream (Fed. Cir. 2008)
- Muniauction v Thomson Corp. (Fed. Cir. 2008)
- Aventis Pharma v Lupin Ltd. (Fed. Cir. 2007)
- Eisai Co. v Dr. Reddy's Labs (Fed. Cir. 2008)
- Proctor & Gamble Co. v Teva (Fed. Cir. 2009)
- Altana Pharma v Teva (Fed. Cir. 2009)

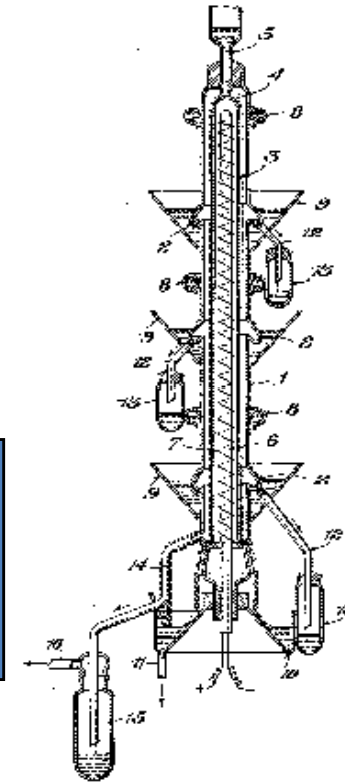


# In re Fout (675 F2d 297; CCPA 1992)

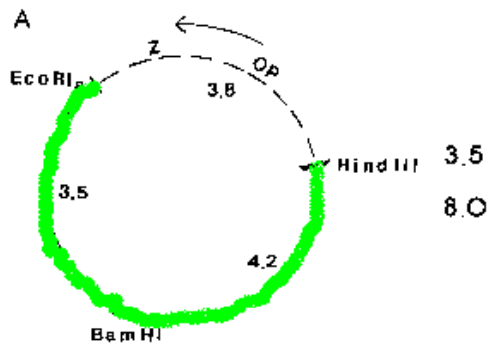
prior art: regeneration of fatty decaffeinating agent  
by **aqueous extraction** (Pagliaro, US 4,465,699)

prior art: extraction of caffeine from oil by **evaporative distillation** (Waterman, US 2,129,596)

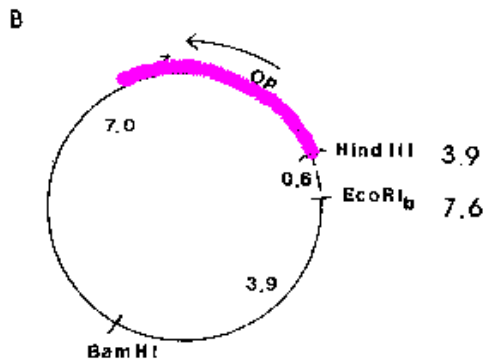
unpatentable: regeneration of fatty decaffeinating agent by substituting **evaporative distillation** for **aqueous extraction** (US appl'n 762,734)



# In re O'Farrell (853 F2d 894; FC 1988)



**prior art: method for  
protein synthesis  
using plasmids  
by Polisky  
(73 PNAS 3900; 1976)**



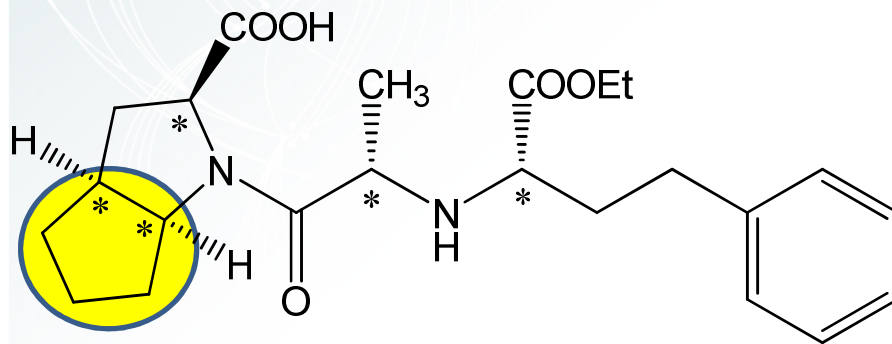
**prior art: method for  
DNA insertion into  
plasmid by Bahl  
(1 Gene 81; 1976)**

**unpatentable:  
protein synthesis  
using DNA insertions  
into plasmid  
(US appl'n 180,424)**

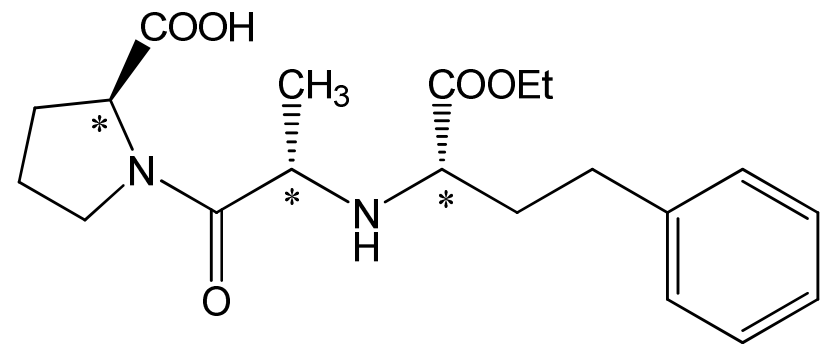
# Aventis v. Lupin

499 F.3d 1293 (Fed. Circ. September 11, 2007)

- ramipril (Altace), for blood pressure
- contains 5 stereocenters, all “S” configuration
- prior art = enalapril (3 stereocenters, all “S”)



ramipril



enalapril

# Aventis v. Lupin

- prior art (Schering) synthesized a mixture of 5S isomer with SSSSR isomer of ramipril
- prior art (Merck, etc) disclosed previous ACE inhibitors with all “S” stereochemistry, including enalapril, with SSS having stronger activity than SSR isomer
- prior art (Schering) disclosed separation of ramipril isomers by chromatography or crystallization
- since KSR, no need for an explicit teaching in the prior art to purify the 5S isomer from a mixture: obvious
- Aventis failed to show unexpected results to rebut



# Aventis v. Lupin

- 2010 KSR Guidelines “teaching point”

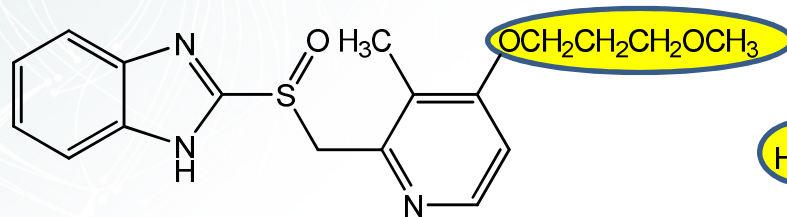
“A chemical compound would have been obvious over a mixture containing that compound as well as other compounds where it was known or the skilled artisan had reason to believe that some desirable property of the mixture was derived in whole or in part from the claimed compound, and separating the claimed compound from the mixture was routine in the art.”



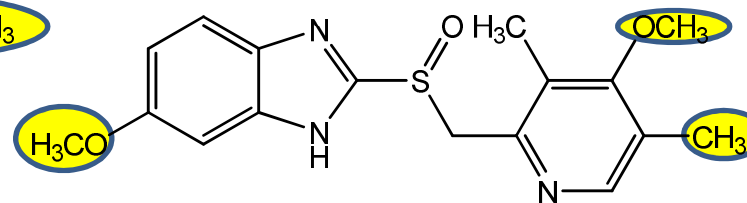
# Eisai v. Dr. Reddy's Labs

533 F.3d 1353 (Fed. Circ. July 21, 2008)

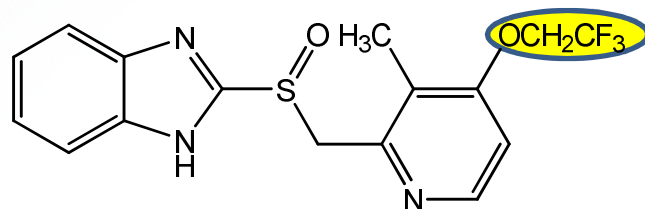
- rabeprazole (Aciphex); PPI for ulcers, GERD
- prior art = lansoprazole, omeprazole, Brändström



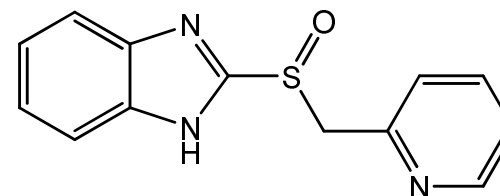
rabeprazole



omeprazole



lansoprazole



Brändström's core



# Eisai v. Dr. Reddy's Labs

- Dr. Reddy's claimed rabeprazole was obvious because of lansoprazole, omeprazole and Brändström's core
- prior art (lansoprazole) contained a  $\text{CF}_3$  group in order to increase lipophilicity, but rabeprazole has no F's
- omeprazole not structurally similar enough
- no "reasoned identification of a lead compound" since the F's were removed, so lansoprazole not a valid lead because no motivation to select it
- no other support to select leads other than lansoprazole
- thus, not obvious to make rabeprazole



# Eisai v. Dr. Reddy's Labs

- 2010 KSR Guidelines “teaching point”

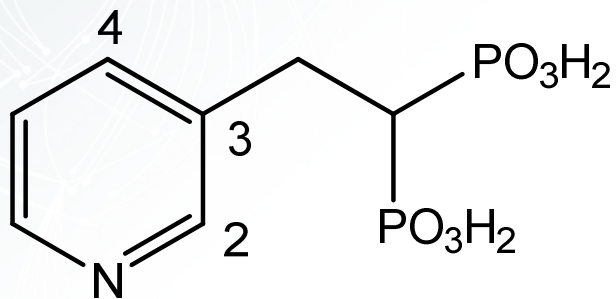
“A claimed compound would not have been obvious where there was no reason to modify the closest prior art lead compound to obtain the claimed compound and the prior art taught that modifying the lead compound would destroy its advantageous property. Any known compound may serve as a lead compound when there is some reason for starting with that lead compound and modifying it to obtain the claimed compound.”



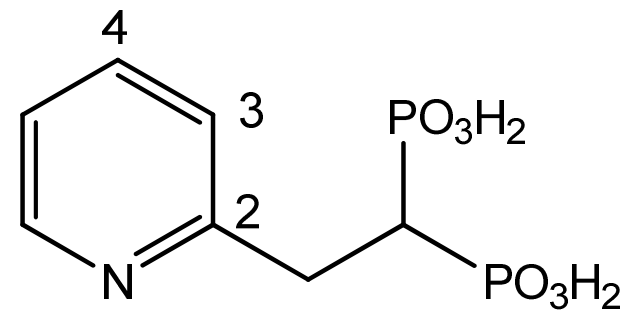
# Proctor & Gamble v. Teva

566 F.3d 989 (Fed. Circ. May 13, 2009)

- risedronate (Actonel); osteoporosis
- 3-pyridyl EHDP



risedronate



prior art

# Proctor & Gamble v. Teva

- prior art = 2-pyridyl EHDP
- bisphosphonate art at the time was very unpredictable
- 3-pyr EHDP much less toxic, 4-pyr EHDP not active
- CAFC: no evidence that the structural modification was routine in the art, so no prima facie case of obviousness
- even if a prima facie case had been shown, the unexpected results would successfully rebut
- secondary considerations (commercial success and meeting a long-felt need) supported nonobviousness



# Proctor & Gamble v. Teva

- 2010 KSR Guidelines “teaching point”

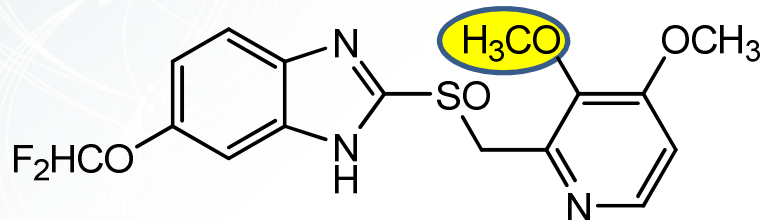
“It is not necessary to select a single compound as a “lead compound” in order to support an obviousness rejection. However, where there was reason to select and modify the lead compound to obtain the claimed compound, but no reasonable expectation of success, the claimed compound would not have been obvious.”



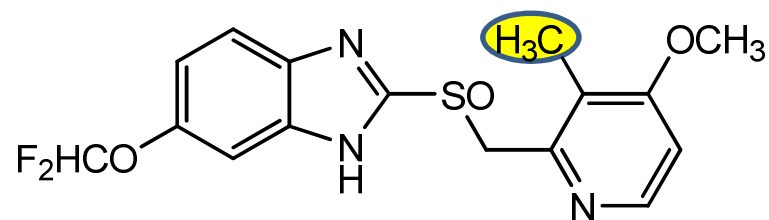
# Altana v. Teva

566 F.3d 999 (Fed. Circ. May 14, 2009)

- pantoprazole (Protonix); PPI for ulcers, GERD
- 3-methoxy pyridine group; prior art = 3-methyl



pantoprazole



prior art

# Altana v. Teva

- prior art compound was identified as one of the “more potent” of 18 compounds for which data was given
- additional prior art (Sachs) taught that the optimum pKa for PPI = 4
- additional prior art (Bryson) taught that the pKa of 3-methoxy pyridine is closer to 4 than the pKa of 3-methyl pyridine
- CAFC: prior art compound was a reasonable lead compound from which to pursue further development
- lower court’s decision for sufficient case of obviousness on merits was affirmed (i.e., likelihood of success)
- Newman concurrence: evidence doesn’t establish obviousness, but deference to lower court given in a preliminary injunction phase



# Altana v. Teva

- 2010 KSR Guidelines “teaching point”

“Obviousness of a chemical compound in view of its structural similarity to a prior art compound may be shown by identifying some line of reasoning that would have led one of ordinary skill in the art to select and modify a prior art lead compound in a particular way to produce the claimed compound. It is not necessary for the reasoning to be explicitly found in the prior art of record, nor is it necessary for the prior art to point to only a single lead compound.”



# MPEP §2143 Rationale B: Practice Tips

B. Simple substitution of one known element for another to obtain **predictable** results.

(i.e.  $A_{\text{known}} \Rightarrow A'$ )

To address an obviousness rejection:

- don't try to patent a particular single isomer of a racemic mixture or mixture of stereoisomers if it's known that the particular single isomer has the desired activity, or use a really non-routine method to do the separation
- try to find prior art that indicates your modification will cause the compound to lose all desired activity
- don't use a known lead compound to start from, combined with known modifications



# MPEP §2143 Rationale B: Practice Tips, continued

B. Simple substitution of one known element for another to obtain **predictable** results.

To address an obviousness rejection:

- if you have used a known lead compound and known modifications, argue that there's no reasonable expectation of success for the claimed compound's activity
- argue that the known compound/set of compounds would not have been selected as "lead" compounds by the skilled artisan, or that there was no motivation in the prior art to make the specific modification



# MPEP §2143, Rationale E

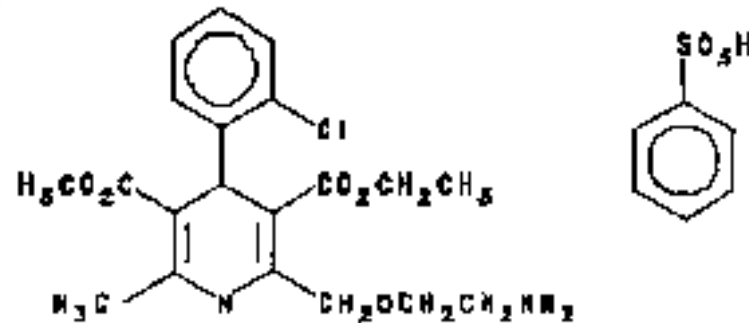
- Nine cases are profiled in Rationale E of the MPEP and 2010 KSR Guideline Update
  - Pfizer v Apotex (Fed. Cir. 2007)
  - Alza v. Mylan Laboratories (Fed. Cir. 2006)
  - Takeda Chem v Alphapharm (Fed. Cir. 2007)
  - Ortho-McNeil v Mylan Labs (Fed. Cir. 2008)
  - Sanofi v Apotex (Fed. Cir. 2008)
  - Bayer v Barr (Fed. Cir. 2009)
  - In re Kubin (Fed. Cir. 2009)
  - Rolls Royce v United Technologies (Fed. Cir. 2010)
  - Perfect Web v InfoUSA (Fed. Cir. 2009)



# Pfizer v. Apotex

480 F.3d 1348 (Fed. Circ. 2007)

prior art: list of 53 FDA-approved  
anions useful for making  
pharmaceutically-acceptable  
salts of drugs  
(Berge, J. Pharm. Sci., 1977)



amlodipine besylate (Norvasc®)

invalid: finite number of pharmaceutically acceptable salts known,  
for a reasonable expectation of success (US 4,879,303)

# Pfizer v. Apotex

- Claim 1 of U.S. Patent No. 4,879,303 recites: the besylate salt of amlodipine.
- Background: At the time of the invention, amlodipine was known as was the use of besylate anions. Amlodipine was known to have the same therapeutic properties as were being claimed for the amlodipine besylate but Pfizer discovered that the besylate form had better manufacturing properties (e.g., reduced “stickiness”). Amlodipine besylate is sold in tablet form in the U.S. under the trademark Norvasc®.



# Pfizer v. Apotex

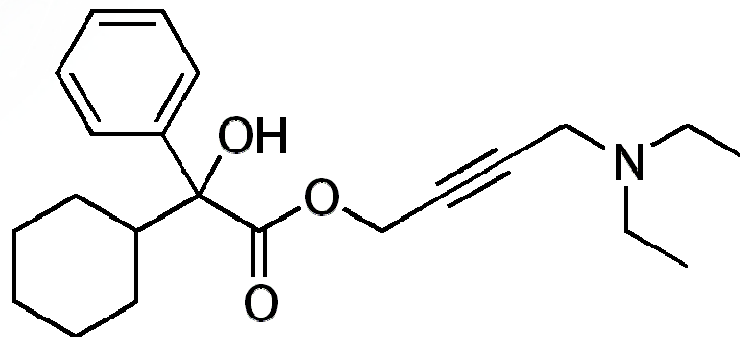
- DC: not obvious
- FC: obvious as it was obvious to try
- Pfizer argued that the results of forming amlodipine besylate would have been unpredictable and therefore nonobvious. The court rejected the notion that unpredictability could be equated with nonobviousness here, because there were only a finite number (53) of pharmaceutically acceptable salts to be tested for improved properties.



# Alza v. Mylan

464 F.3d 1286 (Fed. Cir. 2006)

- Claimed invention: sustained-release formulations of the drug oxybutynin in which the drug is released at a specified rate over a 24-hour period.
- For overactive bladder



Oxybutynin (Ditropan)

# Alza v. Mylan

- “Obvious to try” is not mentioned. However, Alza v. Mylan is used as an example of “obvious to try” rationale in MPEP §2143(E).
- Oxybutynin was known to be highly water-soluble. The specification pointed out that development of sustained-release formulations of such drugs presented particular problems.



# Alza v. Mylan

- (1) Prior art patent to Morella taught sustained-release compositions of highly water-soluble drugs, as exemplified by a sustained-release formulation of morphine. Morella had also identified oxybutynin as belonging to the class of highly water-soluble drugs.
- (2) Patent to Baichwal taught a sustained-release formulation of oxybutynin with a different release rate than the claimed invention.
- (3) Patent to Wong taught a generally applicable method for delivery of drugs over a 24-hour period.
  - Although Wong mentioned applicability of the disclosed method to several categories of drugs to which oxybutynin belonged, Wong did not specifically mention its applicability to oxybutynin.”



# Alza v. Mylan

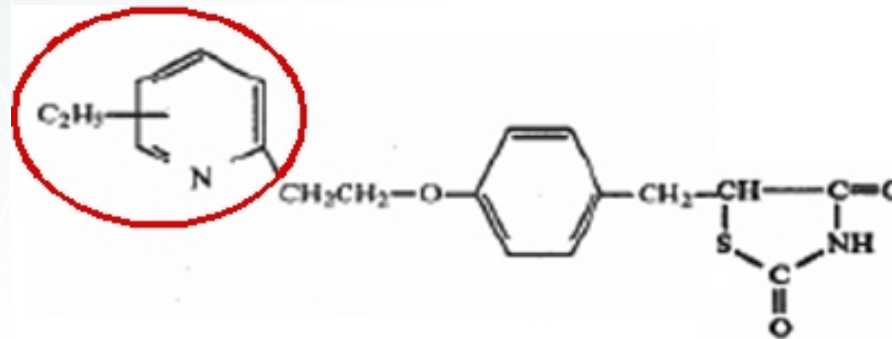
- Federal Circuit: Because the absorption properties of oxybutynin would have been reasonably predictable at the time of the invention, there would have been a reasonable expectation of successful development of a sustained-release formulation of oxybutynin as claimed.



# Takeda Chem v. Alphapharm

492 F.3d 1350 (Fed. Cir. June 28, 2007)

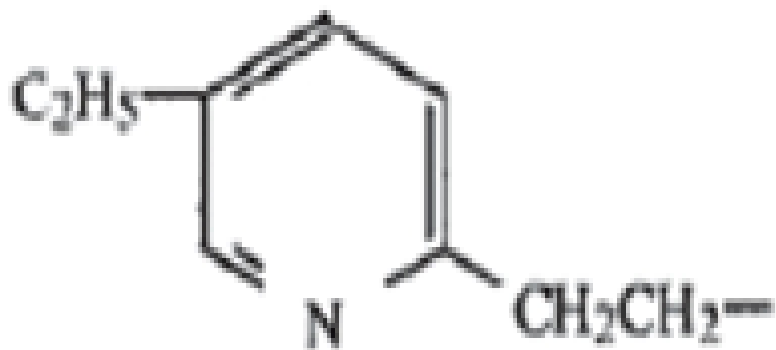
- Claim 1 recites:



- The ethyl-substituted pyridyl ring encompasses four possible compounds as the ethyl substituent (C<sub>2</sub>H<sub>5</sub>) is located at one of four available positions on the pyridyl ring.

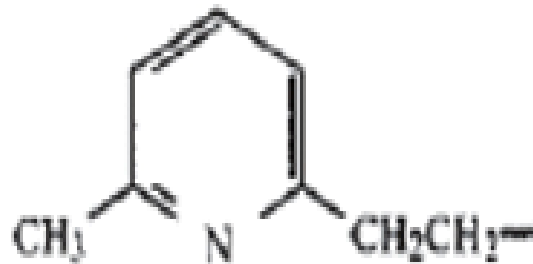
## Takeda Chem v. Alphapharm

- Claim 2 covers pioglitazone (the 5-ethyl compound) which has the ethyl substituent attached at the 5-position of the pyridyl ring



# Takeda Chem v. Alphapharm

- Alphapharm asserted that the claimed compounds were obvious based on a prior art compound known as “compound b.” Compound b possesses a pyridyl ring in which a methyl ( $\text{CH}_3$ ) group is attached to the 6-position:



# Takeda Chem v. Alphapharm

- District Court concluded that “there was no motivation in the prior art to select compound b as a lead compound for antidiabetic research, and that the prior art actually taught away from its use.”
- DC also concluded that even if Alphapharm had succeeded in making a *prima facie* case of obviousness, such a showing would be rebutted by the unexpected results of pioglitazone's nontoxicity.



# Takeda Chem v. Alphapharm

- DC and FC: nonobvious
- FC's analysis:
  - Alphapharm failed to show that Compound b would have been selected as the lead compound
  - Alphapharm failed to show a reason to modify Compound b to achieve the claimed compounds.



# Takeda Chem v Alphapharm

- 2010 KSR Guidelines “teaching point”

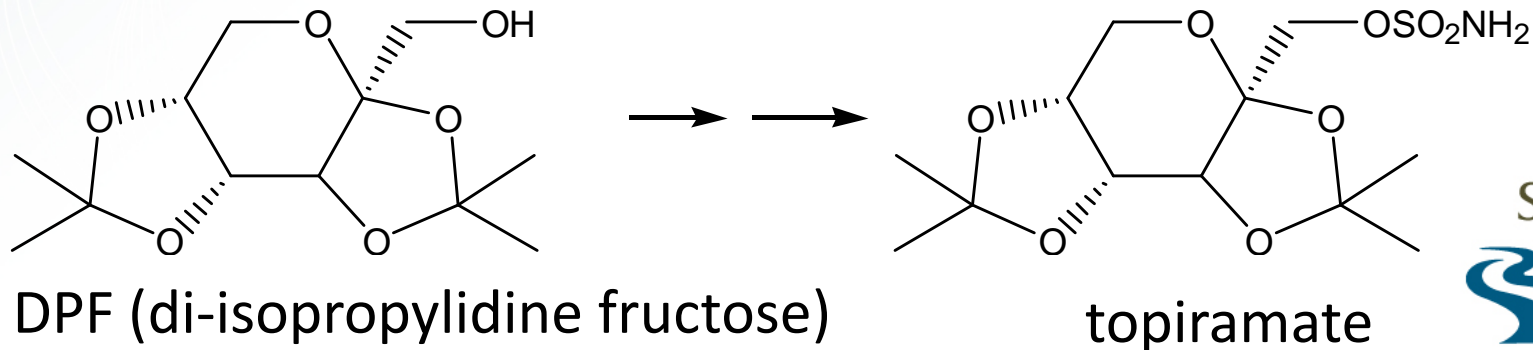
“A claimed compound would not have been obvious where it was not obvious to try to obtain it from a broad range of compounds, any one of which could have been selected as the lead compound for further investigation, and the prior art taught away from using a particular lead compound, and there was no predictability or reasonable expectation of success in making the particular modifications necessary to transform the lead compound into the claimed compound.”



# Ortho-McNeil v. Mylan Laboratories

Fed. Cir. March 31, 2008

- topiramate (Topomax); epilepsy drug
- lower court permanently enjoined Mylan from infringing Ortho's product, and the FC affirmed
- Ortho was searching for new diabetes drugs, but found that a synthetic intermediate (itself derived from DPF) for an anti-diabetic compound was a potent anticonvulsant



## Ortho-McNeil v. Mylan

- CAFC: a skilled artisan “would not even be likely” to start with DPF as a lead compound to design a diabetes drug
- hindsight analysis is inappropriate
- the subject matter as a whole must be examined at the time the invention was made; not obvious
- secondary considerations also support nonobviousness
  - powerful unexpected results
  - skepticism of experts and copying
  - commercial success



# Ortho-McNeil v Mylan

- 2010 KSR Guidelines “teaching point”

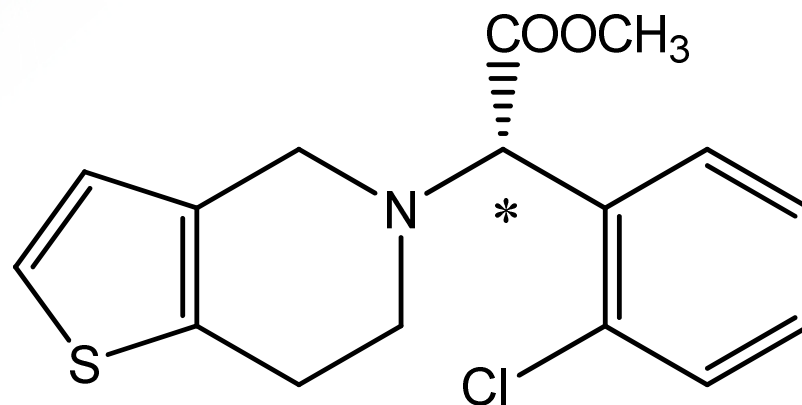
“Where the claimed anti-convulsant drug had been discovered somewhat serendipitously in the course of research aimed at finding a new anti-diabetic drug, it would not have been obvious to try to obtain a claimed compound where the prior art did not present a finite and easily traversed number of potential starting compounds, and there was no apparent reason for selecting a particular starting compound from among a number of unpredictable alternatives.”



# Sanofi v. Apotex

Fed. Circ. December 12, 2008

- clopidogrel bisulfate (Plavix); blood thinner
- single enantiomer
- prior art = racemic mixture



# Sanofi v. Apotex

- CAFC: the separation of the mixture was not routine or simple (salt with (+)-camphorsulfonic acid/acetone)
- Apotex cited no reference that showed or suggested a reliable method of separation for analogous compounds
- success in the separation was unpredictable
- unknown before the separation which isomer desirable
- KSR recognized hindsight bias as inappropriate
- not obvious to separate the enantiomers



# Sanofi v Apotex

- 2010 KSR Guidelines “teaching point”

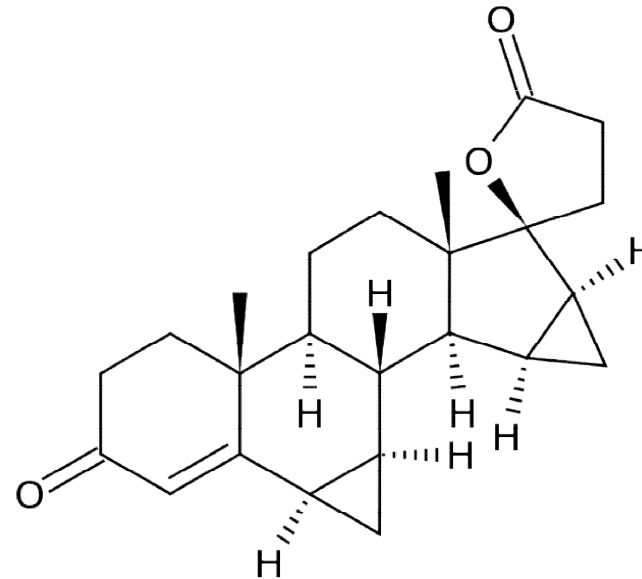
“A claimed isolated stereoisomer would not have been obvious where the claimed stereoisomer exhibits unexpectedly strong advantages over the prior art racemic mixture without the correspondingly expected toxicity, and the resulting properties of the enantiomers separated from the racemic mixture were unpredictable.”



# Bayer v. Barr

Fed. Circ. August 5, 2009

- drospirenone (Yasmin); oral contraceptive
- poorly soluble in water
- isomerizes in acid to a compound with undesired properties



# Bayer v. Barr

- prior art taught micronization to improve solubility in water, but it also increased acid sensitivity
- enteric coatings known to protect oral drugs from stomach acid, but also decreased bioavailability
- Bayer found that the micronized drug with an enteric coating had same bioavailability as without the coating
- CAFC; prior art narrowed options to a finite number of identifiable predictable solutions, so obvious
- Newman dissent; no reasonable expectation of success here



# Bayer v Barr

- 2010 KSR Guidelines “teaching point”

“A claimed compound would have been obvious where it was obvious to try to obtain it from a finite and easily traversed number of options that was narrowed down from a larger set of possibilities from the prior art, and the outcome of obtaining the claimed compound was reasonably predictable.”



# In re Kubin

561 F.3d 1351 (Fed. Circ. 2009)

- Claims directed to polynucleotide (cDNA) encoding a particular polypeptide (hNAIL protein)
  - NK Cell Activation Inducing Ligand (NAIL)
  - NK cells target and kill diseased cells and recruit other immune cells
  - NAIL is a cell surface marker or receptor which modulates the activity of NK cells.
- Exemplary Claim:
  - An isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide at least 80% identical to amino acids 22-221 of SEQ ID NO:2, wherein the polypeptide binds to CD48.



# In re Kubin

- Court recognizes dual nature of nucleic acids, moves them away from treating nucleic acids solely under a chemical structural obviousness analysis
- Court indicates that, given the factual circumstances, claimed invention was “profoundly predictable” due to specific teachings in prior art and advancements into cloning and sequencing technologies
- Subsequent decisions by Board of Patent Appeals & Interferences have emphasized that “generalized” motivations to experiment in a given field are not sufficient to meet the “obvious to try standard”
- Post-Kubin decisions from Board of Patent Appeals & Interferences also emphasize absolute predictability not required to support obviousness
  - Only a reasonable expectation of success is required
  - Specific motivation/encouragement from prior art may become a surrogate for the requisite “reasonable expectation of success”



# In re Kubin

- 2010 KSR Guidelines “teaching point”

“A claimed polynucleotide would have been obvious over the known protein that it encodes where the skilled artisan would have had a reasonable expectation of success in deriving the claimed polynucleotide using standard biochemical techniques, and the skilled artisan would have had a reason to try to isolate the claimed polynucleotide. KSR applies to all technologies, rather than just the “predictable” arts”



# MPEP §2143 Rationale E: Practice Tips

E. “Obvious to try” – choosing from a finite number of identified, **predictable** solutions, with a reasonable expectation of success  
(i.e. **A - Z** => obvious to try; **A - ∞** => invention)

To address an obviousness rejection:

- argue that the prior art did not present a finite or easily traversed number of potential possibilities. For example, argue that there is an immense number of possible starting compounds.



# MPEP §2143 Rationale E: Practice Tips

E. “Obvious to try” – choosing from a finite number of identified, **predictable** solutions, with a reasonable expectation of success

(i.e. **A - Z** => obvious to try; **A - ∞** => invention)

To address an obviousness rejection:

- argue that there was not a “lead” compound known in the prior art, no reason to select any particular starting compound as a “lead” or that the prior art taught away from using a particular lead compound
- argue that there was no predictability or reasonable expectation of success of making the claimed compound from the prior art lead compound



# MPEP §2143 Rationale E: Practice Tips

- E. “Obvious to try” – choosing from a finite number of identified, **predictable** solutions, with a reasonable expectation of success  
(i.e. **A - Z** => obvious to try; **A - ∞** => invention)

To address an obviousness rejection:

- (if applicable) argue that the single isomer exhibits unexpectedly strong therapeutic advantages over the prior art racemic mixture without the expected toxicity, or that the resulting properties of the single isomer are unpredictable compared to the racemic mixture



# Summary of Recent Drug “Structural Similarity” Obviousness Cases

case	date	holding
Takeda v. Alphapharm	2007	<p><b>not obvious</b></p> <ul style="list-style-type: none"> <li>- prior art taught away from compound b</li> <li>- no reason to select it as a lead</li> <li>- unexpectedly non-toxic</li> </ul>
Ortho-McNeil v. Mylan	2008	<p><b>not obvious</b></p> <ul style="list-style-type: none"> <li>- no reason to select cmpd as a lead</li> <li>- no reason to test it as anticonvulsant</li> <li>- unpredictable result</li> </ul>
Eisai v. Dr Reddy's Labs	2008	<p><b>not obvious</b></p> <ul style="list-style-type: none"> <li>- no reason to select cmpd as a lead</li> <li>- prior art taught away from F's</li> </ul>



# Continued Summary of Recent Drug “Structural Similarity” Obviousness Cases

case	date	holding
Altana v. Teva	2009	nonobviousness not determined - lead compound identified in prior art - one of only 18 cmpds disclosed - <b>likely</b> that the lead compound would have been selected for modification
Proctor & Gamble v. Teva	2009	<b>not obvious</b> - no reason to select cmpd as a lead - no reason to modify that cmpd - unexpected results



# Summary of Recent Drug Salt Obviousness Cases

case	date	holding
Pfizer v. Apotex*	March, May 2007	<b>obvious</b> <ul style="list-style-type: none"><li>- besylate known in art</li><li>- finite number of anions known (53)</li><li>- obtained via routine testing</li></ul>



# Summary of Recent Drug Isomer Obviousness Cases

case	date	holding
Aventis v Lupin (5(S) isomer from mixture)	2007	<b>obvious</b> -multi-(S) stereochemistry known for better activity - conventional methods to do the separation
Sanofi v Apotex (separation of D,L isomers from racemic mixture)	2008	<b>not obvious</b> -unknown which isomer had better activity -unpredictable because after separation, one isomer had all the bio activity and the other had all the toxicity



# Summary of Recent Drug Formulation Obviousness Cases

case	date	holding
Alza v. Mylan (sustained release)	2006	<b>obvious</b> - finite number of solutions in the prior art - reasonable expectation of success
In re Omeprazole (adding a subcoating)	2008	<b>not obvious</b> - problem not known - no known motivation to address problem - solution was known but not applied to that problem
Bayer v. Barr (removing a coating)	2009	<b>obvious</b> - finite number of options to test - predictable outcome





# General Practice Tips



# Practice Tips for Preparing Application

- Continue to avoid unnecessary characterizations of the invention by:
  - Omitting background section
  - Omitting recitation of objects of the invention and a summary of the invention
- When unnecessary for utility purposes, do not reference a particular problem faced by the inventor(s) or solved by the inventor(s)
  - Applications nationalized from Europe should be scrutinized for such references and the references should be deleted upon filing.



# *Prima Facie* Case of Obviousness

- If possible, assert that the examiner has failed to establish a *prima facie* case of obviousness
  - Always try to overcome rejection before rebutting obviousness.
  - For compounds, PTO must first establish structural obviousness. Unexpected properties can then be used to overcome rejection.
- Make sure that examiner has specified rationale and set forth facts that support rationale.
- No hindsight reconstruction



# Guaranteed (almost) winners (still)

- Teaching away (but no stretching!)
- Modification renders prior art unsatisfactory for intended purpose
- Modification changes the principle of operation of a reference
- Combined references lack an element recited in claim (unless common sense or ordinary creativity fills in the gaps)



# Lack of Predictability (A-F)

- Except for the TSM test, all rationales (A-F) relate to predictability.
  - So argue the invention is not predictable!
  - Argue no reasonable expectation of success
  - Argue that elements work together in an unexpected way.



# TSM

- If the TSM test is used, you can still argue that there is no suggestion or motivation to combine the prior art references or to make modifications.
  - Don't assume that TSM rationale was used and do not automatically frame response with typical TSM arguments.



# Assess PHOSITA

- If reasonable, and if it does not present any complications for your positions with respect to 35 U.S.C. 112 ¶ 1, argue that the PHOSITA has a low level of skill in the art and would not have been able to combine the prior art references to reach the claimed invention.
- When identifying the PHOSITA's level of skill in the art, remember that the skill of the actual inventor is not necessarily relevant.
- Factors to be considered in identifying the level:
  - Educational level of the inventor and others in the field
  - Technology field of the invention
  - Nature of the problems encountered in the field
  - Previous solutions to the problem or related problems



# General Prosecution Suggestions - Longer Shots

- Analyze prosecution history of prior art reference to find “teaching away” or evidence of lack of predictability
- Consider asserting that the prior art is nonanalogous.
  - While this approach is often very difficult, it should not be overlooked.
- Secondary considerations
  - Long-felt, unmet need; failure of others; etc.



# Declarations

- Present a fact-based analysis of obviousness
- While declarations are still excellent fodder in litigation, the facts established via declarations are increasingly critical for overcoming obviousness rejections and there may not be another choice.
- So consider a declaration to address issues such as “unexpected results”, “teaching away” and the unpredictability of the combination to the skilled artisan as these issues are questions of fact.



# Interviews

- Try to always interview the examiner
  - Meet with the examiner in person
  - If necessary, reach agreement on data to be submitted in declaration that overcomes rejection by showing unexpected results, lack of predictability, secondary considerations, problems in the art, level of skill, etc.



# For More Information



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