

Getting the Best Patent Protection for Bioproducts from a Changing Patent Office

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The Patent Application Process

- ▶ Patent applications filed with the U.S. Patent and Trademark Office
 - Claims define the invention
- ▶ USPTO examines applications for:
 - Novelty (is the invention new?)
 - Non-obviousness (would it have been obvious?)
 - Enablement (does the application show how to make and use the invention?)
 - Other requirements

The Patent Application Process

- ▶ Examiner allows or rejects the claims
- ▶ Applicants can amend claims, or provide arguments or evidence that rejection is incorrect
- ▶ No limits (or very few) on:
 - Continuations
 - Number of claims
 - Language and Chemical Formulas used in claims

The Changing Patent Office

- ▶ Backlog of applications waiting for examination
- ▶ Long pendency - 25 months to first action
- ▶ Vocal critics
 - “bad” patents being issued
 - unlimited continuations create uncertainty

USPTO's Response to Backlog & Criticisms

- ▶ Proposed Rules (none are final yet)
 - Limits on continuations & claims
 - Shifts burden of searching to applicants
 - Limits on use of chemical formulas
- ▶ Too aggressive?
 - On April 1, 2008, a federal judge enjoined the USPTO from limiting continuations and claims
- ▶ More aggressive with obviousness rejections
- ▶ Reluctance by examiners to allow applications

What is “Obviousness”?

- ▶ If an invention would have been obvious, it's not patentable
 - When? At the time of the invention
 - Who? To a person of ordinary skill in the art
 - Compared to what? Prior art patents, publications, knowledge, sales, etc.
- ▶ US Supreme Court lowered the standard (*KSR v. Teleflex*)
 - Easier for USPTO to reject claims for obviousness

USPTO Guidelines on Obviousness

- ▶ Rationales that support obviousness rejection
 - Logic that justifies putting the pieces together
- ▶ **Predictability** is overarching theme
 - Were known techniques used to make predictable improvements?
 - Does the new process yield predictable results?

USPTO's Rationales Of Obviousness

- ▶ Combining prior art elements according to known methods to yield **predictable** results;
- ▶ Simple substitution of one known element for another to obtain **predictable** results;
- ▶ *In re O'Farrell*, 853 F.2d 894 (Fed. Cir. 1988)
 - Claims to method of synthesizing a protein in a transformed bacteria
 - Obvious to replace one heterologous gene with another

USPTO's Rationales Of Obviousness

- ▶ Use of known technique to improve similar products in the same way
- ▶ "Obvious to try" – choosing from a finite number of identified, **predictable** solutions, with a reasonable expectation of success

“Obvious to Try”

- ▶ *Pfizer v. Apotex*, 480 F.3d 1348 (Fed. Cir. 2007)
 - Claim to amlodipine besylate was obvious based on (1) amlodipine and (2) use of besylate anions
 - Finite number of identified, predictable solutions: 53 anions
- ▶ **Salt forms no longer patentable?**
 - Look for biological difference – would be truly unexpected
 - Identify any synergies, challenges in manufacture or screening, ingenuity in selection
 - Explain why the salt or its properties were not predictable

“Obvious to Try”

▶ *ALZA v. Mylan*, 464 F.3d 1286 (Fed. Cir. 2006)

- Reasonable expectation of successful development of sustained release oxybutynin

2. A sustained-release oxybutynin formulation for oral administration to a patient in need of treatment for urge incontinence comprising a therapeutic dose of an oxybutynin selected from the group consisting of oxybutynin and its pharmaceutically acceptable salt that delivers from 0 to 1 mg in 0 to 4 hours, from 1 mg to 2.5 mg in 0 to 8 hours, from 2.75 to 4.25 mg in 0 to 14 hours, and 3.75 mg to 5 mg in 0 to 24 hours for treating urge incontinence in the patient.

▶ **Controlled release formulations not patentable?**

- Is it more than a release rate of active agent?
- Is it more than combining known drug in known platform?

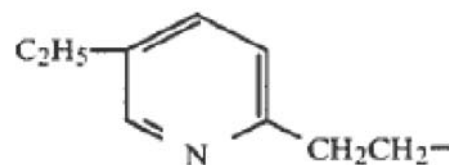
“Obvious to Try”

- ▶ *In re Kubin*: Isolated nucleic acid was obvious from prior art disclosing encoded polypeptide
 - problem was to isolate a specific nucleic acid
 - known methods of sequencing were used by the applicants
- ▶ **Nucleic acid sequences encoding known proteins no longer patentable?**
 - May depend on particular facts
 - Was it a technical achievement to obtain the sequence?

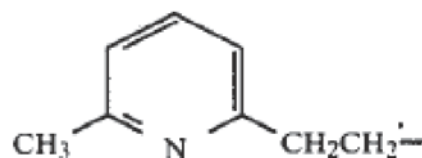
New Chemical Entities

▶ *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007)

– Pioglitazone (ACTOS)



– Prior art: “compound b”



– **Not obvious:** teaching away & unexpected properties (compound b was toxic, pioglitazone was not)

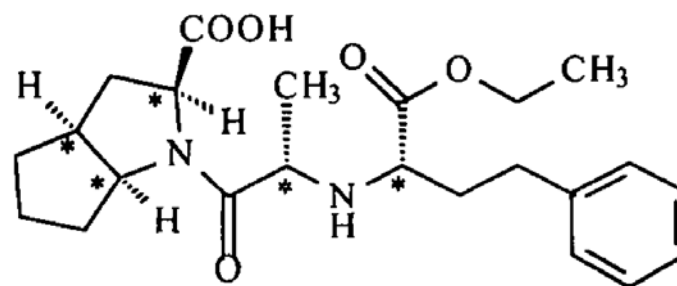
– Practice Tip: identify differences in structure and in properties, and why properties are unexpected

Obvious Enantiomers

▶ *Aventis Pharma Deutschland GmbH v. Lupin*, 499 F.3d 1293 (Fed. Cir. 2007)

– Ramipril (ALTACE):

▶ 5(S) enantiomer



– Prior art:

▶ same compound in racemic mixture (SSSSS and SSSSR)

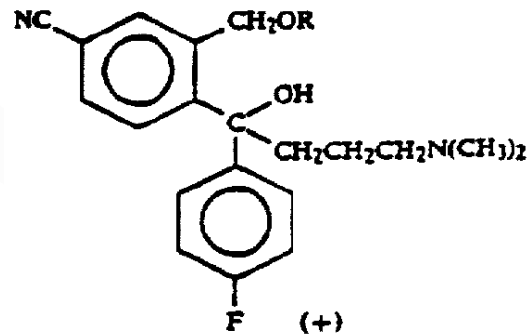
▶ similar compound → SSS was 700-fold more potent than SSR

– **Obvious:** POSITA would know how to separate enantiomers and would expect benefit

Patentable Enantiomers

- ▶ *Forest Labs. v. IVAX & Cipla*, 501 F.3d 1263 (Fed. Cir. 2007)

- escitalopram
 - ▶ LEXAPRO
 - ▶ S- or (+) -



- **Not Obvious:**
 - ▶ difficulty of separating the enantiomers, and unexpected property: therapeutic benefit expected in R- citalopram rather than S- citalopram
- Practice Tip: identify reasons why separation of enantiomers was not routine and/or why properties of particular enantiomer were not expected

Recognize the Series of Innovations in the Life Cycle of a Bioproduct

- ▶ What innovations are most likely to be considered nonobvious?
 - Salt forms → difficult to make? unexpected biological properties?
 - Separated enantiomers → separation techniques known? expectation that one has benefit?
 - Polymorphs → considered unpredictable
 - Formulations → “platform” formulation or something new?
 - Combinations → Is there synergy?
 - Methods of Treatment → preclinical data?
 - Dosing → clinical data?

Information to be Included in Applications

- ▶ Identify new structures, properties & functions
 - Especially **therapeutic properties**, but others too
 - Identify departures from “conventional techniques”
- ▶ Include more examples & data
- ▶ Do not trivialize inventor’s recognition of the problem
- ▶ Identify **synergies**
 - Synergy: $2 + 2 = 5$ or more

Planning for Future Inventions

- ▶ May want to avoid “poisoning the well”
 - Usual practice: comprehensive & predictive
 - What additional research is underway?
 - Balance & judgment

- ▶ What innovations are most likely to be nonobvious?
 - New Chemical Entities
 - Novel Polypeptides
 - Stereoisomers
 - Polymorphs
 - Methods of Treatment
 - Others

Discussion Questions & Answers



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Thank you!

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