



# **Obviousness in View of KSR TC1600-Specific Examples**

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# Post-KSR Cases

- **U.S. Court of Appeals for the Federal Circuit**
- **U.S. District Court for the Southern District of New York**
- **Board of Patent Appeals and Interferences**



# U.S. Court of Appeals for the Federal Circuit

- **Takeda Chemical Industries v. Alphapharm Pty, Ltd., 492 F.3d 1350, 83 USPQ2d 1169 (Fed. Cir. 2007)**
- **Pharmastem Therapeutics, Inc. v. Viacell, Inc., 491 F.3d 1342, 83 USPQ2d 1289 (Fed. Cir. 2007)**



# U.S. District Court for the Southern District of New York

- **In re Omeprazole Patent Litigation, 490 F. Supp. 2d 381 (S.D. N.Y. June 1, 2007)**
- **McNeil-PPC, Inc. v Perrigo Company, [cite] (S.D. N.Y. June 5, 2007)**





# Board of Patent Appeals and Interferences

- **Ex parte Kubin, 83 USPQ2d 1410 (Bd. Pat. App. & Int. 2007)**



# Takeda v. Alphapharm

- **Defendant filed ANDA to market generic version of pioglitazone (ACTOS®) – diabetes 2 treatment**
- **Plaintiff owns patent to pioglitazone and sued for infringement in District Court (S.D. N.Y.)**



# Takeda v. Alphapharm

- **Defendant asserted invalidity based on obviousness**
- **District Court concluded patent valid**
- **Defendant appealed to the Federal Circuit**



# Takeda v. Alphapharm

## □ Claim

□ **Pioglitazone – a thiazolidinedione (TZD) with an ethyl-substituted pyridyl ring at the 5-position**

## □ Prior Art

□ **Reference teaching “compound b”, which differs from pioglitazone by having a methyl in place of ethyl in the 6-position, instead of the 5-position**



# Takeda v. Alphapharm

- **Defendants' Theory of Obviousness**
  - **"Compound b" was known to be an effective anti-diabetic compound**
  - **Homologation and ring-walking were within the skill of one of ordinary skill in the art**
  - **It would have been obvious to modify "compound b" via homologation and ring-walking in order to produce another compound with anti-diabetic activity**



# Takeda v. Alphapharm

## □ Plaintiffs' Rebuttal

- **No reason to choose "compound b" out of "hundreds of millions of TZD compounds" in the prior art disclosure**
- **Review article of 101 TZD compounds (including "compound b") teaches away from "compound b"**
- **Unexpected reduced toxicity of pioglitazone compared to "compound b"**



# Takeda v. Alphapharm

- **Court Rationale**
  - ❑ **No “finite number of identifiable, predictable solutions”**
  - ❑ **Prior art provided “broad selection of compounds”**
  - ❑ **Closest prior art compound exhibited negative properties**
- **Holding**
  - ❑ **Patent valid – compound nonobvious**



# Pharmastem v. Viacell

- **Plaintiff owned patents to cryopreserved umbilical cord blood**
- **Defendants provided service of cryopreservation of umbilical cord blood**
- **Plaintiff alleged infringement**
- **Defendants asserted invalidity**





# Pharmastem v. Viacell

## □ Claims

- **A cryopreserved therapeutic composition comprising umbilical cord blood hematopoietic stem cells**
- **A method for hematopoietic or immune reconstitution comprising cryopreserving of umbilical cord blood hematopoietic stem cells, thawing, and administering to a human**



# Pharmastem v. Viacell

## □ **Prior Art**

- **Knudtzon reference**
- **Ende reference**
- **Prindull reference**
- **Koike reference**
- **Vidal reference**
  
- **All prior art references discuss the presence of stem cells in cord blood**



# Pharmastem v. Viacell

- **Defendants' Theory of Obviousness**
  - **?** Prior art identified the presence of stem cells in umbilical cord blood (Admissions in spec, Prindull)
  - **?** Prior art taught that stem cells in umbilical cord blood could be cryopreserved and thawed (Koike, Vidal)
  - **?** Prior art suggested the use of stem cells for transplantation (Vidal, Ende, Knudtson)



# Pharmastem v. Viacell

- **Plaintiffs' Rebuttal**
  - ❑ **Prior art used "flawed nomenclature"**
  - ❑ **No reasonable expectation of success based on prior transplants of analogous stem cells (blood, marrow)**
  - ❑ **Long-felt need**
  - ❑ **Commercial success**



# Pharmastem v. Viacell

- **Court's rationale**
  - ❑ **Could not reconcile expert testimony with statements in the specification**
  - ❑ **Did not agree with expert that terminology was "flawed"**
  - ❑ **Prior art references to "stem cells" were consistent with Applicants' statements in the specification**
  - ❑ **Citing KSR, determined that invention was confirmation of what was already believed to be true**



# Pharmastem v. Viacell

## □ **Holding**

- **Patent invalid – method and composition obvious**

## □ **Dissent – Judge Newman**

- **Majority engaged in impermissible hindsight**
- **Ignored peer response**
- **Ignored jury verdict**
- **Ignored scientific experts**
- **Ignored agency expertise**



# Highlights and Guidance

- **Evidence is critical to the determination of obviousness**
  - **Court in Takeda focused on “teaching away” and unexpected results**
  - **Court in Pharmastem focused on Applicants’ statements in specification**



# In re Omeprazole

- **Plaintiff Astrazeneca filed multiple infringement suits against several generic manufacturers based on ANDAs for omeprazole (Prilosec®)**
- **Defendants asserted invalidity on multiple theories including obviousness**





# In re Omeprazole

## □ Claim

- A formulation comprising
- (a) a core comprising omeprazole plus an alkaline reacting compound (ARC);
- (b) an inert subcoating, which is soluble or rapidly disintegrates in water, disposed on the core region,
- (c) an outer layer disposed on the subcoating comprising an enteric coating



# In re Omeprazole

## □ **Prior Art**

- **References disclosed a core with a subcoating and enteric coating but did not disclose omeprazole**
- **References disclosed omeprazole but did not disclose a subcoating or an alkaline reacting compound**
- **References described subcoatings and techniques but did not disclose omeprazole**



# In re Omeprazole

- **Defendants' Theory of Obviousness**
  - ❑ **Prior art disclosed that acid labile pharmaceuticals are conventionally subcoated and coated**
  - ❑ **Prior art disclosed that it conventional to use subcoatings**
  - ❑ **Prior art disclosed that it was conventional to use an ARC**



# In re Omeprazole

- **Court's Rationale**
  - ❑ **Prior art compounds that were subcoated and coated were not comparable to omeprazole**
  - ❑ **Prior art compounds that were subcoated and coated were delivered to different part of the GI tract**
  - ❑ **Prior art disclosure to omeprazole formulations did not disclose stability problems**



# In re Omeprazole

- **Court's Rationale, continued**
  - ❑ **References taught away from subcoated formulation**
  - ❑ **Expert testimony of "multitude of possible paths and dead-ends" in formulation attempts**
  
- **Holding**
  - ❑ **Patent valid – formulation unobvious**



# McNeil-PPC v Perrigo

- **Plaintiffs filed infringement suit based on ANDAs filed by Defendants on combination of famotidine and antacids (Pepcid<sup>®</sup> Complete)**
- **Defendants assert invalidity based on the theory of obviousness**



# McNeil-PPC v Perrigo

- **Claim**
  - ❑ **Solid oral dosage form comprising**
    - ❑ **(a) coated famotidine granules**
    - ❑ **(b)  $\text{Al}(\text{OH})_3$  or  $\text{Mg}(\text{OH})_2$  granules**
  - ❑ **Wherein the coating on the famotidine is impermeable to the  $\text{Al}(\text{OH})_3$  or  $\text{Mg}(\text{OH})_2$**



# McNeil-PPC v Perrigo

## □ **Prior Art**

- ❑ **Reference disclosed combination of uncoated histamine H<sub>2</sub> receptor antagonists and antacids**
- ❑ **References disclosed coating granulated medicaments to mask taste of active ingredient**
- ❑ **Reference acknowledged the bitter taste of cimetidine**





# McNeil-PPC v Perrigo

- **Defendants' Theory of Obviousness**
  - ❑ **All relevant limitations of the claim appeared in the prior art**
  - ❑ **One of ordinary skill in the art would have coated the famotidine in the prior art combination formulation to mask the bitter taste of famotidine**



# McNeil-PPC v Perrigo

## □ Plaintiffs' Rebuttal

- There was no suggestion that the combination formulation in the prior art was bitter, therefore there was no reason to coat the famotidine alone
- Other modes of taste-masking were preferable due to cost of coated granules



# McNeil-PPC v Perrigo

- **Court's Rationale**
  - ❑ **The combination of coated famotidine and the antacids provided no more than predictable results, citing KSR**
  - ❑ **Costs alone are not indicative of non-obviousness**
  
- **Holding**
  - ❑ **Patent invalid – formulation obvious**



# Highlights and Guidance

- **Recognition of problems in the prior art as well as answers to problems in the prior art may lead to a finding of obviousness**
  - ❑ **In McNeil, single problem is solved with predictable results**
  - ❑ **In Omeprazole, numerous variables suggested that the results would not be predictable**



# Ex parte Kubin

## □ 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 CD48**



# Ex parte Kubin

## □ Prior Art

- Reference disclosed p38 protein (same protein as NAIL) and methods of isolation by using mAbs as well as methods of obtaining the polynucleotide sequence but does not disclose the sequence of p38
- Reference disclosed the nucleic acid sequence of the highly conserved murine version of p38 and identified a human homologue



# Ex parte Kubin

- **Examiner's Arguments**
  - **One of ordinary skill in the art would have been motivated to apply conventional methodologies to isolate and identify the cDNA sequence of human NAIL in view of the teachings of the prior art**



# Ex parte Kubin

- **Appellants' Arguments**
  - ❑ **Cited references did not provide adequate written description of cDNA of NAIL**
  - ❑ **Reliance on In re Deuel – knowledge of a protein does not render obvious the cDNA encoding it**
  - ❑ **No motivation to combine the references**





# Ex parte Kubin

- **Board's Rationale**
  - ❑ **State of the art has advanced**
  - ❑ **Reliance on KSR – “obvious to try” in view of limited methodologies available to isolate NAIL cDNA**
  - ❑ **Methodologies had reasonable expectation of success**



# Highlights and Guidance

- **Advancements in the state of the art may render that which was once unpredictable to become predictable**



# Thank You!

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