Overcoming §103 Rejections for Biotech and Chemical Patents: Leveraging Recent Decisions and USPTO Guidance

THURSDAY, JUNE 9, 2016

1pm Eastern | 12pm Central | 11am Mountain | 10am Pacific

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STRADDLING March 15/16, 2013

Enactment: Sept. 16, 2011

PCT Filing

Pre-AIA § 103 applies to all claims

Priority Date

Scenario 1: no claims entitled to priority date:
Scenario 2: all claims entitled to priority date:
Scenario 3: mixed EFD claims March 15/16, 2003

PCT Filing

Scenario 1: AIA § 103 applies to all claims
Scenario 2: Pre-AIA § 103 applies to all claims
Scenario 3: AIA § 103 applies to all claims

Priority Date

Effective Date: March 16, 2013

Scenario 1: AIA § 103 applies to all claims
OLD: 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.

NEW: A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains.
PRE-AIA § 103

- Applicable to patents/applications with all claims with effective filing date before March 16, 2013.
- Pre-AIA §102 definitions of prior art.
- As of date of invention

AIA § 103

- Applicable to patents/applications with at least one claim with an effective filing date after March 15, 2013 (includes JMM applications!)
- New §102 definitions of prior art: BIG CHANGE.
- As of effective filing date of invention: BIG CHANGE.
The question of obviousness is resolved based on underlying factual determinations identified in *Graham*.

This includes addressing the differences between claimed subject matter and the prior art,

Addressing whether there is a reason to combine art (*KSR*), and

Avoiding conclusory statements.


At issue: Federal Circuit's ruling that a patent may not be found invalid for obviousness unless the prior art sets forth a “teaching, suggestion, or motivation” to combine the prior art teachings in the manner claimed in the patent.

USSC: Claim obvious. Reverse and remand.
   · Graham analysis reaffirmed.
Graham v. John Deere Co.,
383 U.S. 1 (U.S. 1966)

◦ “[if] the difference between the subject matter sought to be patented and the prior art... would have been obvious at the time to a person skilled in the art, then the subject matter cannot be patented.”

◦ Satisfying § 103 is legal question with factual underpinnings:

- the scope and content of the prior art;
- differences between the prior art and the claims at issue; and
- the level of ordinary skill in the pertinent art.
- And “[s]uch secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., ... may have relevancy.”
WHAT **KSR** AND **AIA**
**DID NOT CHANGE**

- *Graham* remains the basic test for AIA obviousness.
- Reasonable expectation of success still required for obviousness.
- Teaching away by the prior art may support a finding of non-obviousness.
- Objective evidence of non-obviousness such as unexpected results, failures of others, long-felt but unmet need, or commercial success may be important although may not overcome a strong prima facie case of obviousness.
- Hindsight analysis is improper.
MOTIVATION TO COMBINE MAY BE DIFFERENT

  - Product claim: 0.2% B + 0.5% T
  - Method claim: reducing number of daily doses of claimed product from 3 to 2.
  - Prior art: serial administration of .02-2% (family of B) and .01-3% (T)
  - Prior art suggested motivation to combine to increase patient compliance.
  - DC: Claims not invalid for obviousness.
    - Patient compliance not FDA factor for approval;
    - formulation arts unpredictable;
    - some teaching away in the prior art; and
    - secondary considerations supported non-obviousness
MOTIVATION TO COMBINE MAY BE DIFFERENT

Allergan v. Sandoz (con’t)

• FC: Reversed-in-part -> product claims obvious.
  
  – Motivation to combine may be found beyond FDA considerations; here, found in the prior art.

  – Reasonable expectation of success based on prior art.
    – problems developing commercial product irrelevant.

  – Prior art “as a whole” did not teach away, and district court failed to consider impact on clear motivation to combine.

  – Secondary factors do not merit much weight.
MOTIVATION TO COMBINE MAY BE DIFFERENT

- Allergan v Sandoz (con’t)
    - Prior art showed loss of efficacy when dosage at 2x/day rather than 3x/day.
    - Prior art shows administration of B+T at same time, and 2x/day, but does not show no loss of efficacy.
    - Failure to show obviousness by clear and convincing evidence.
    - Judge Dyk would have held method claim obvious too.
      - Just newly-discovered property, not newly-discovered method of use.
In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litigation, 676 F.3d 1063 (Fed. Cir. 2012)

- FC: Patent on an extended-release formulation of a muscle relaxant is not invalid for obviousness despite its bioequivalence with a prior immediate-release version.

  - Without a known PK-PD relationship at the time of invention, "skilled artisans could not predict whether any particular PK profile, including a bioequivalent one, would produce a therapeutically effective formulation."
NOT OBVIOUS TO TRY

Sanofi-Aventis Deutschland GmbH v. Glenmark Pharmaceuticals Inc., USA, 748 F.3d 1354 (Fed. Cir. 2014)

• ANDA litigation relating to Tarka®
  — combination of a double-ring ACE inhibitor with calcium antagonists

• DC: Valid and infringed.

• FC: Affirmed.
Sanofi (con’t)

- FC:
  - Analogous to *Pozen Inc. v. Par Pharmaceutical, Inc.*, 696 F.3d 1151 (Fed. Cir. 2012), where court sustained a patent on a previously unknown combination of known compounds that was found to have longer-lasting efficacy than either component separately.

  - A POSITA at the time of the invention “would not have predicted the longer-lasting hypertension control demonstrated by the double-ring structures of quinapril and trandolapril in combination with calcium antagonists, because of the widespread belief that double-ring inhibitors would not fit the pocket structure of the ACE.”
NON-OBJUSNESS OF RANGES

Allergan, Inc. v. Sandoz Inc., 796 F.3d 1293 (Fed. Cir. 2015)

• Claims drawn to compositions and methods of lowering intraocular pressure in a patient with open-angle glaucoma or ocular hypertension comprising about 0.01% bimatoprost and about 200 ppm benzalkonium chloride.

• Prior art disclosed formulation comprising 0.001%-1% bimatoprost and 0-1000 ppm benzalkonium for treating glaucoma.
Allergan, Inc. v. Sandoz Inc. (con’t)

• FC:

  – “district court did not clearly err in finding that the prior art taught away from a formulation comprising 0.01% bimatoprost and 200 ppm BAK, and that such a formulation exhibited unexpected results.”

  – “The record thus shows that the prior art ‘criticize[d], discredit[ed], or otherwise discourage[d]’ the use of 200 ppm BAK in a bimatoprost formulation.”
NON-OBJUSINESS OF RANGES

Allergan, Inc. v. Sandoz Inc. (con’t)

• FC:

  “Although the prior art does not teach that particular combination of amounts of bimatoprost and BAK, those amounts do fall within the ranges disclosed in a single reference .... As we explained in Galderma, where there is a range disclosed in the prior art, and the claimed invention falls within that range, a relevant inquiry is whether there would have been a motivation to select the claimed composition from the prior art ranges. ...In those circumstances, ‘the burden of production falls upon the patentee to come forward with evidence that (1) the prior art taught away from the claimed invention; (2) there were new and unexpected results relative to the prior art; or (3) there are other pertinent secondary considerations.’”
NON-OBVIOUSNESS OF RANGES

Allergan, Inc. v. Sandoz Inc. (con’t)

• FC:

— “in this case, the prior art ranges are broader than the range in Galderma, and the record shows that the claimed amounts of the two different ingredients could and did materially and unpredictably alter the property of the claimed formulation.”

— “This is not a case where the claims merely recite the unknown properties of an otherwise obvious formulation....Here, the previously unknown and unexpected properties of a new and nonobvious formulation constitute additional, objective evidence of nonobviousness.”
REMINDER OF DIFFERENT BURDENS

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<td>Claim construction</td>
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<td>Phillips/Markman framework: analyze claims, specification, and prosecution history to determine how claims would be understood by one of ordinary skill in the art</td>
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INSTITUTION RATE FOR BIO/PHARM PETITIONS LOWER THAN OVERALL RATE


NEARLY 40% OF THE BIO/PHARMA INSTITUTION DECISIONS HAVE BEEN DENIALS

Patent Owner’s best outcome is a denial
BASIS FOR PETITION DENIAL IN BIO/PHARMA IPRS

Failed to meet threshold, 94, 85%

Time bar, 5, 4%
RPI, 3, 3%
Claim construction, 1, 1%
325d, 8, 7%

Source: Finnegan research;
111 petition denials as of April 22, 2016.
WHEN DOES PATENT OWNER HAVE CHANCE TO PERSUADE PTAB TO DENY INSTITUTION?
INSTITUTION DECISION
NON-APEALABLE MAKING DENIAL HIGHLY DESIRABLE FOR PATENT OWNER

• 35 U.S.C. § 314(d): NO APPEAL.—The determination by the Director whether to institute an inter partes review under this section shall be final and nonappealable.

USE THE POPR

Challenge the Petitioner’s asserted lead compound as a starting point with arguments such as:

• Failure to show that there is some kind of superior performance over other starting points;

• Lack of a desirable characteristic (or presence of an undesirable characteristic) compared to other potential starting points;

• More complicated modification required than the development from other potential starting points;

• No explanation of how the particular modification would be selected.
OTHER ARGUMENTS FOR POPR

- Level of unpredictability in the art.
- Degree of expectation of success associated with some of the starting points available to a POSITA.
PETITION DENIALS: SUCCESSFUL USE OF LEAD COMPOUND ARGUMENT
LEAD COMPOUND ANALYSIS

Helps to guard against impermissible hindsight that may arise when a primary prior art reference is selected by identifying a structurally similar compound to the claimed compound, and then proposing suitable modifications of that compound to arrive at the claimed compound.

Structural similarity alone does not explain why a person of ordinary skill in the art (POSITA), representing a hypothetical person presumed to have been aware of all pertinent prior art at the time of the invention, would have selected the most structurally similar compound as a starting point for further development.
PTAB IS USING LEAD COMPOUND ANALYSIS

2-part test set out in *Otsuka Pharmaceutical Co., Ltd. v. Sandoz, Inc.*, 678 F.3d 1280 (Fed. Cir. 2012)

- (1) Determine whether a chemist of ordinary skill would have selected the asserted prior art compounds as lead compounds, or starting points, for further development efforts; and

- (2) then determine whether the prior art would have supplied one of ordinary skill in the art with a reason or motivation to modify a lead compound to make the claimed compound with a reasonable expectation of success.

Apotex challenged Merck’s claims to a genus of tachykinin receptor antagonists useful in treating inflammatory diseases, pain or migraine, asthma, and emesis.

• Prior art disclosed a genus of tachykinin receptor antagonists, and listed 601 specific compounds as within the scope of that genus.

• A secondary reference purportedly provided the motivation to use phosphoramidate prodrugs to modify the parent compound of fosaprepitant (disclosed as one of the 601 compounds in the primary reference) to arrive at the claimed invention.
Patent Owner Preliminary Response: a POSITA would not have looked to the primary reference to develop tachykinin receptor antagonists, and even if a POSITA did, it would not have picked the one specific compound from the list of 601.

- Also presented evidence of prior art discussion at the time of the invention of more promising lead compounds.
PTAB: Petition denied.

- Petitioner had not explained why a person of ordinary skill in the art would have picked that one compound for further development out of a list of 600 specific compounds disclosed in the prior art.

- Even the preferred substituents disclosed in the prior art included hundreds of possible options.

- Not only would a POSITA have had to select each of the substituents of the asserted lead compound, it would have had to select all of them at the same time.
Sawai challenged Nissan’s claims to mevalonolactone derivatives having a quinoline ring and their use as a pharmaceutical for reducing hyperlipidemia, hyperlipoproteinemia, or atherosclerosis.

- A secondary reference allegedly provided the motivation to a POSITA to modify Petitioner’s lead compound, Picard Example 3, to achieve the claimed compound.

PTAB: Petition denied.

- Petitioner failed to show evidence of any particular functional activity to suggest that the compound should serve as a lead compound. Rather, the data disclosed in the Picard reference related to a compound significantly different from Picard Example 3.

- It appeared Petitioner’s selection of Picard Example 3 was based on structural similarity, which, by itself, is not enough to inform the lead compound selection.

- Even assuming that Picard Example 3 was an appropriate starting point, Petitioner did not explain adequately why one would have chosen the particular modification required.
Representative claim 1. A compound represented by Formula (I):

Prior art (Fenton):

Prior art (Ashton):
PTAB: Petition denied.

• Petitioner argued that Fenton’s ‘hierarchy of preferred substituents’ at the positions of $R_1$, $R_2$, $R_3$, $Z_1$, $Z_2$, and $Z_3$ would have led one skilled in the art to the exact compound recited in claim 1.”

• “Petitioner’s arguments are tenuous at best. In order to illustrate our reasoning, however, we treat them as if they were correct. Even with such a head start, Petitioner cannot meet its burden. A proper obviousness inquiry analyzes the differences between the prior art and the claimed invention as a whole. ...Here, even assuming, as Petitioner contends, one skilled in the art would have chosen, separately, difluoromethyl at $R_1$, cyclopropylmethyl at $R_2$, 3,5-dihalopyrid-4-yl N-oxide at $R_3$, oxygen at both $Z_1$ and $Z_2$, and CONH- at $Z_3$, Petitioner has not sufficiently explained why one skilled in the art would have selected the claimed substituents at each of the six independent positions all at once.”


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PTAB: Petition denied (con’t)

- Attempted lead compound argument failed also because Petitioner did not explain why a POSITA would have selected two compounds as lead compound from the list of 147 exemplary compounds. “Moreover, Petitioner does not provide any evidence or reasoning as to why a skilled artisan would have modified those two compounds to arrive at the claimed compound.”
PETITION DENIALS:
PATENT OWNER PERSUADES
PTAB THAT PETITIONER FAILED
TO PROVIDE REASONABLE BASIS
FOR POSITA TO COMBINE/MODIFY
THE ASSERTED REFERENCES
Patent Owner argued that Petitioner failed “to provide any reasonable basis for how or why a person of skill in the art would have combined” the prior art references.

PTAB: Petition denied.

• “We agree with Patent Owner. ...What is missing from Petitioner’s challenge, however, is an explanation of how the ordinary artisan would have modified the method of Horigane 1, wherein multiple seeds are ground simultaneously, to prevent cross-contamination of protein and DNA between the seeds, as required by the method disclosed by Sangtong. ... None of the remaining proffered references cure that deficiency.”
PTAB: Petition denied.

- Petitioner failed to meet threshold showing of obviousness.
  - No explanation why a POSITA would have modified the teachings of the references to arrive at the claimed invention.
  - Insufficient explanation how the references may be combined to arrive at the claimed invention.
    - For example, in one reference, the post-grinding seed surface is analyzed, in another it is the ground material removed from the seeds is analyzed.
PTAB: Petition denied (con’t)

• “We find that Petitioner does not present sufficient articulated reasoning with rational underpinning to support a conclusion of obviousness. ... [R]eliance on Keller for a reason to combine the references is unavailing.”

• “Petitioner also does not explain adequately why a person of ordinary skill in the art would have modified the teachings of the Horigane references with the teachings of Kelley and CN2510248 Y, to arrive at the subject matter of claim 55.”
PTAB: Petition denied.

- PTAB would not accept Petitioner’s explanation as to why POSITA would have been motivated to combine the prior art references found in declaration but not petition.

  - “we are not persuaded that the Petition has advanced a rational underpinning sufficient to support the obviousness challenges”
  - Petition fails to identify the specific teachings in the references “that would have prompted an ordinary artisan to use [prior art] mutant MspA’s in Akeson’s system.”
  - “the Petition does not identify any clear or specific teaching in the cited prior art, or in the knowledge available to an ordinary artisan, explaining why an ordinary artisan would have considered a mutated porin having that property desirable, or even useful, in Akeson’s system.
  - Petition did not explain how modification was a predictable use of a prior art element according to its established function.
Phigenix, Inc. v. Genentech, Inc.,

Patent Owner:

• Neither the Petition nor the expert declaration “adequately explains how, or provides sufficient evidence indicating that, the teaching in HERCEPTIN® Label that certain patients failed to respond to HERCEPTIN® would have motivated an ordinary artisan to treat [claimed patient population] using a HERCEPTIN® (huMab 4D5-8) conjugate.”
PTAB: Petition denied.

• Petitioner “does not establish a reasonable likelihood that it would prevail in showing that an ordinary artisan would have had reason to use the recited conjugate, i.e., one containing the HERCEPTIN® antibody, to treat ErbB2 receptor-overexpressing tumors in patients (or mammals) that failed to exhibit a complete or partial response rate when treated with the antibody in the non-conjugate form.”

• Persuaded by Patent Owner’s evidence that a POSITA would have thought it likely that HERCEPTIN® resistance occurred in patients because obstacles prevented HERCEPTIN® from working as expected.
  — “The Petition and Dr. Rosenblum do not explain why an ordinary person skilled in the art would have thought HERCEPTIN® would be a good choice, rather than ‘a particularly poor choice for an immunoconjugate to treat such patients.’”

• The HERCEPTIN® Label “identifying” patients that do not respond, or respond poorly, to an anti-ErbB antibody does not teach or suggest how to treat such patients, much less teach or suggest treating such patients with an anti-ErbB antibody conjugate.” (emphasis added)
PTAB: Petition denied.

• “Notably absent from BioGatekeeper’s stated rationale, however, is a sufficient explanation of how or why teachings in the references would have been combined, from the perspective of one with ordinary skill in the art, to arrive at the claimed invention.”
PTAB: Petition denied.

- Generalities insufficient.

  “The information presented by BioGatekeeper may be sufficient to establish that each of the genes recited in claim 1 were known; however, the Petition lacks sufficient information to support a determination that a person of ordinary skill in the art would have had a reasonable expectation of success in achieving pluripotency of a mammalian stem cell using the specific combination of genes recited in claim 1. At best, the Petition directs us to general guidance in the prior art with regard to particular genes involved in cell differentiation and cell division, but fails to point us to specific guidance as to how, for example, the recited genes would function together at the appropriate developmental stage of the cells to achieve pluripotency. ... Such general guidance as provided in the Petition does not establish a reasonable likelihood that Petitioner would show the requisite “reasonable expectation” of success ....”
PTAB: Petition denied.

• Insufficient evidence of motivation to modify reference or to combine references.
  
  – Expert declarations “merely parrot the argument presented in the Petition. ... They also are unsupported by sufficient evidence.”

  – Expert declaration conclusion inconsistent with reference, and did not explain.

  – “For purposes of this Decision, we assume, without deciding, as Petitioner asserts, highly conserved genes are attractive targets for species-specific identification. Petitioner, however, does not argue that rpoB is the only, or even one of a finite number of conserved genes in MTB. Petitioner does not offer any persuasive evidence to show why one of ordinary skill in the art would have chosen rpoB, instead of any other conserved genes, to develop a method for species-specific identification.”
PTAB: Petition denied.

- “even assuming that an ordinary artisan would have selected PMPA/tenofovir as a lead compound for further modification, Petitioner does not persuade us” that a POSITA would have modified the references “so as to arrive at a compound encompassed by the challenged claims.”

- Insufficient explanation why POSITA would choose a particular ester: “Petitioner does not persuade us that Cheng’s esters would have been recognized by one of ordinary skill in the art as a generally accepted strategy...for improving the bioavailability of any drug having a phosphonic acid moiety, regardless of therapeutic activity, or other structural attributes.”

- “in view of the shortcomings and unpredictability in the prodrug strategies in the cited references, as well as the lack of specific teachings in Tsai, Cheng, Srinivas, and Kubo leading an ordinary artisan to the particular compounds recited in the challenged claims, we are not persuaded that Petitioner has established a reasonable likelihood of prevailing in showing that the challenged claims would have been obvious to that artisan.”

Petitioner: “it would have been obvious, and there would have been a reasonable expectation of success for a person of skill in the art to formulate...the known bis(poc)PMPA, with fumaric acid to make the fumarate salt form of bis(poc)PMPA.”

• “development of a salt form of Bischofberger’s bis(POC)PMPA would have been ‘essential’ or ‘required’ for FDA approval of the drug; and
• one of ordinary skill in the art would have turned to Takashima for guidance in developing the requisite salt form, as that reference provides a short list of candidate counterions for use with compounds similar to bis(POC)PMPA."

Patent Owner:
• No requirement to have a salt for a successful oral pharmaceutical;
  – Provided evidence of FDA-approved non-salt pharmaceutical.
• No reference indicates need to create a salt form of [(R)-bis(POC)PMPA]; and
• Reference “does not disclose any PMPA-based compound, much less a POC derivative of PMPA.”
PTAB: Petition denied.

- “Neither Petitioner nor Petitioner’s Declarant, Dr. Fisher, provides evidence or argument sufficient to substantiate these assertions.”

- No explanation of connection between references such that a POSITA would have looked to one to solve the problem of the other.
Petitioner: “given the references’ teachings, an ordinary artisan “would have found it obvious and would have had a reasonable expectation of success in 1996 of making a poc prodrug of tenofovir, i.e., a bis(poc) prodrug of tenofovir, to increase oral bioavailability and enable clinical acceptance of tenofovir as a prophylactic and therapeutic drug for HIV infection.”

PTAB: Petition denied.

- Insufficient showing that “the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention.”
USE OF DECLARATIONS TO PROVIDE FOUNDATION FOR DENIAL

- Build up specification and file history during drafting and prosecution.
  - Solidify novelty, non-obviousness, enablement, and written description positions.
  - Consider declarations during prosecution, but be mindful of inequitable conduct attacks in litigation.

- Declarations need to be as solid as possible. PTAB has found that defective declarations relied on for patentability during prosecution can form an independent basis for instituting an IPR.
    - Board reviewed a § 1.131 declaration from the prosecution, found it deficient, and reapplied the prior art the declaration had antedated, instituting the IPR.
    - Case also had live testimony from inventor at oral hearing.
    - One might want declarations from the inventor during prosecution that can then be referred to by the Patent Owner in the optional Preliminary Response to try to ward off institution.
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<th>Final Rule 42.107</th>
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<td><strong>(a)</strong> The patent owner may file a preliminary response to the petition. The response is limited to setting forth the reasons why no <em>inter partes</em> review should be instituted under 35 U.S.C. 314. The response can include evidence except as provided in paragraph (c) of this section. . . .</td>
<td><strong>(a)</strong> The patent owner may file a preliminary response to the petition. . . . The response <em>is limited to setting</em> forth the reasons why no <em>inter partes</em> review should be instituted under 35 U.S.C. 314 <em>and can include supporting evidence.</em></td>
</tr>
<tr>
<td><strong>(c)</strong> <em>No new testimonial evidence.</em> The preliminary response shall not present new testimony evidence beyond that already of record, except as authorized by the Board.</td>
<td><strong>(c)</strong> [RESERVED]</td>
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(c) Sufficient grounds. *Inter partes* review shall not be instituted for a ground of unpatentability unless the Board decides that the petition supporting the ground would demonstrate that there is a reasonable likelihood that at least one of the claims challenged in the petition is unpatentable. The Board's decision will take into account a patent owner preliminary response where such a response is filed, including any testimonial evidence, but a genuine issue of material fact created by such testimonial evidence will be viewed in the light most favorable to the petitioner solely for purposes of deciding whether to institute an inter partes review. A petitioner may seek leave to file a reply to the preliminary response in accordance with §§ 42.23 and 42.24(c). *Any such request must make a showing of good cause.*
OBJECTIVE EVIDENCE OF NONOBVIOUSNESS: USE EVIDENCE FROM PROSECUTION
OBJECTIVE EVIDENCE IN “RECORD” SUCCESSFULLY USED BY PATENT OWNER TO GET PETITION DENIED


- Patent Owner requested PTAB exercise its discretion to deny the petition because of the same art/arguments before the Office during reexamination.

- Patent Owner was able to rely on evidence of commercial success that was in the record of a reexamination proceeding involving the patent.

  - “the Examiner found a prima facie case of obviousness existed during the second Reexamination. ...The Examiner determined that secondary considerations of obviousness overcame the prima facie case.”
OBJECTIVE EVIDENCE IN “RECORD” SUCCESSFULLY USED BY PATENT OWNER TO GET PETITION DENIED

*Omron* (con’t)

– PTAB: Petition denied.

  – Found Petitioner established a prima facie case of obviousness, and then reviewed the objective evidence of nonobviousness provided to the examiner during a reexamination, and agreed that it was persuasive.

  – “we determine that Patent Owner has presented sufficient evidence to establish a prima facie case of nexus.”

  – No rebuttal by Petitioner.

  – “We find that the ’142 Patent had significant commercial success, which, here, overcomes the prima facie case of obviousness.”
NEED TO SHOW NEXUS

*Prometheus Labs., Inc. v. Roxane Labs., Inc.*, 805 F.3d 1092 (Fed. Cir. 2015)

• Claim: 5. A method for treating a diarrhea-predominant female IBS patient, while excluding those with predominant constipation, said method comprising:
  – assessing whether said diarrhea-predominant female IBS patient has experienced symptoms for at least six months; and
  – administering an effective amount of alosetron or a pharmaceutically acceptable derivative thereof to said patient who has experienced symptoms for at least six months, wherein said effective amount is dependent on the condition of the patient and is at the discretion of the attendant physician.
NEED TO SHOW NEXUS

• Prometheus commercial success:

  – Sales revenue increased but increase in number of prescriptions was modest -> marketing and rebates, not the patent, was responsible for commercial success.

  – “Prometheus did not submit an analysis that would show the commercial success for the...patent on its own merits, ‘control[ling] for other variables and separat[ing] the treatment instructions from the drug compound and the method in the ... patent that already existed, nor any analysis to control for other changing variables, such as marketing campaigns, new drug warnings, pricing changes, etc.”
NEED TO SHOW NEXUS

• Prometheus long-felt but unmet need and industry praise.

  — “more likely attributable to ... the new safety precautions, heightened awareness, and warnings issued after Lotronex’s reintroduction.”
NEXUS IS ALSO REQUIRED BEFORE THE PTAB

• Objective evidence of non-obviousness generally not working before the PTAB.

• In many cases, Patent Owners are not having much success with objective evidence of non-obviousness because they are not showing nexus (linking the objective evidence of obviousness to the merits of the claimed invention).
“NEXUS” REQUIRED


— PTAB:

— “Before delving into the specific arguments and evidence of secondary considerations, we note that it is not sufficient that a product or its use merely be within the scope of a claim in order for objective evidence of nonobviousness tied to that product to be given substantial weight. There must also be a causal relationship, termed a ‘nexus,’ between the evidence and the claimed invention. ... A nexus is required in order to establish that the evidence relied upon traces its basis to a novel element in the claim, not to something in the prior art. ...Objective evidence that results from something that is not ‘both claimed and novel in the claim,’ lacks a nexus to the merits of the invention. ...All types of objective evidence of nonobviousness must be shown to have nexus. ...The stronger the showing of nexus, the greater the weight accorded the objective evidence of nonobviousness.”
NO “NEXUS”


- Patent Owner failed to establish nexus between the claimed invention and the objective evidence.

- PTAB:
  - “Any commercial success of the Health Buddy is only relevant if the Health Buddy actually was the claimed monitoring system or apparatus, or actually was used to practice the methods, recited in the challenged claims. Patent Owner has not provided sufficient evidence to show that was the case.”
  - “Patent Owner does not show sufficiently that the ‘192 patent actually satisfied the alleged need. ... Thus, Patent Owner’s evidence of long-felt need is not persuasive.”
  - “Evidence of industry praise is only relevant when it is directed to the merits of the invention claimed. ... Patent Owner has not established a sufficient nexus with the claimed methods, and industry praise of the Health Buddy does not support a conclusion of nonobviousness of the claims.”
NO “NEXUS”


• All challenged claims unpatentable.
• Patent Owner’s objective evidence evidence insufficient.

  – “ConvaTec has not shown, however, that the sales of the AQUACEL® Ag product line are a result of the claimed invention.”

  – “no details of the manufacturing process for AQUACEL® Ag products as supporting evidence that the products are manufactured using the steps recited in the claims.”

  – No explanation:
    – “how such praise is directed to any particular feature of the method recited in the claims.”
    – “that advantages of the claimed invention are not met by silverized hydrogels of the prior art[.]”
    – “that the evidence of long-felt and unmet need is solved by the particular steps recited in the claims, or to the photostability of the product, to the extent they are distinguishable from the prior art of record.”
**NO “NEXUS”**


- Patent Owner argued “the failure of others to mass produce sufficient amounts of [API] to meet the needs created by market demand[.]”
- PTAB: The problem with this argument is that the claims do not require large-scale commercial production or specific levels of purity and yield.

- Patent Owner: Unexpected results of yield and purity.
- PTAB: Post-grant testing “does not reflect the results that would have been expected (or unexpected) at the time of the invention in 1999.
  - no data in the patent to support its claim of unexpected results.
  - “Patent Owner has not met its burden of establishing a nexus between a novel feature of the claimed invention and the unexpected results. For example, Patent Owner has not accounted for the additional unclaimed steps in the Prolastin®-C method, like the dissolution step, which Patent Owner’s declarants admit affect purity and yield.
EXAMPLE WHERE PATENT OWNER SHOWED NEXUS


• PTAB: Claims not unpatentable.

  “Patent Owner cites substantial evidence of objective indicia of non-obviousness in relation to claim 8, which is directed to the T-DM1/Kadcyla® commercial product.

  Evidence of satisfying a long-felt, unmet need for an immunoconjugate capable of targeting a solid tumor in patients without excessive toxicity.

  Evidence of commercial success: sales and prescription data, and marketing and promotional efforts relating to Kadcyla®
EXAMPLE WHERE PATENT OWNER SHOWED NEXUS

- **Phigenix (con’t)**
  - “In view of the specific components recited in claim 8, i.e., a specific antibody, linker, and toxin, which are the same as those in T-DM1/Kadcyla®, we are persuaded that Patent Owner establishes a sufficient nexus in relation to the cited objective evidence of nonobviousness.”

- “The specification of the ‘856 patent discloses, and claim 8 recites, the very components that led to the unexpected results, praise and commercial success....Patent Owner sufficiently establishes that it is the exact combination of those components recited in claim 8, rather than different components previously combined in the prior art, that provided the unexpected results at issue, and led to praise and commercial success.”
EXAMPLE WHERE OBJECTIVE EVIDENCE SUCCESSFULLY USED BY PATENT OWNER TO AVOID UNPATENTABILITY DETERMINATION


• Patent Owner submitted objective evidence of nonobviousness via a declaration (prepared for the IPR) supporting the Patent Owner Response.

• PTAB: Final Written Decision that Intri-Plex did not meet its burden of showing challenged claims unpatentable.
  
    “we determine that the first three Graham factors favor a determination that the challenged claims are obvious. However, a proper obviousness determination requires a consideration of all factors, and we determine that Saint-Gobain’s case for nonobviousness based on secondary considerations is particularly strong, and outweighs the other three factors. In particular, we are persuaded that our finding of commercial success is particularly strong, .... Indeed, we determine that commercial success alone sufficiently outweighs the other three factors, and that our finding of copying merely strengthens further our finding that secondary considerations weigh in favor of Saint-Gobain.”
EXAMPLE WHERE OBJECTIVE EVIDENCE INSUFFICIENT TO AVOID UNPATENTABILITY DETERMINATION


• Claim 19. A solid pharmaceutical composition suitable for oral administration, comprising mannitol and 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol or a pharmaceutically acceptable salt thereof.

• Patent Owner’s objective evidence of nonobviousness:
  – Unexpected results: claimed combination was stable at low doses of fingolimod, even though combinations of fingolimod and other excipients were unstable at those same low doses.

• PTAB: But claim 19 is not limited to any particular dose or dose range of fingolimod.
EXAMPLE WHERE OBJECTIVE EVIDENCE INSUFFICIENT TO AVOID UNPATENTABILITY DETERMINATION

Torrent Pharms (con’t)

• Patent Owner’s objective evidence of nonobviousness: the invention satisfied the long-felt but previously unmet need “for a solid oral [multiple sclerosis] treatment.”

• PTAB: Insufficient.
  – The only evidence submitted as support was a declaration by a witness who was not made available for cross-examination.
  – Credited Petitioner’s argument that the need was satisfied by treatments known but not yet approved.
    – “If objective indicia of nonobviousness are due to an element in the prior art, no nexus exists....Because the prior art contained solid oral multiple sclerosis treatments using active ingredients other than fingolimod, the fingolimod claimed in claim 19 was not necessary to satisfy any long-felt need for a solid oral multiple sclerosis treatment.”
EXAMPLE WHERE OBJECTIVE EVIDENCE INSUFFICIENT TO AVOID UNPATENTABILITY DETERMINATION

Torrent (con’t)

• Patent Owner argued industry praise.

• PTAB: “Industry praise must be linked to the patented invention....Again, if objective indicia of nonobviousness are ‘due to an element in the prior art, no nexus exists.’ Here, the evidence shows that what was praised about Gilenya was not the specific formulation recited in claim 19, but rather the general fact that Gilenya was a solid oral multiple sclerosis medication. ... [H]owever, a solid oral multiple sclerosis formulation was known in the prior art, so there is no nexus between the claimed invention and the industry praise.”
EXAMPLE WHERE OBJECTIVE EVIDENCE INSUFFICIENT TO AVOID UNPATENTABILITY DETERMINATION

Torrent (con’t)

- Patent Owners argued commercial success.

- PTAB: “But commercial success is relevant only when it is due to [something] disclosed in the patent . . . which was not readily available in the prior art.”
  - “Patent Owners bear a burden of production with respect to evidence of commercial success; they must show significant sales in a relevant market, and that the successful product is the invention disclosed and claimed in the patent....If Patent Owners make such a showing, Petitioners may rebut the evidence of commercial success by showing that the commercial success was instead due to other factors extraneous to the patented invention[..]”
EXAMPLE WHERE OBJECTIVE EVIDENCE INSUFFICIENT TO AVOID UNPATENTABILITY DETERMINATION

Torrent (con’t)

• PTAB: Success due to solid oral formulation; irrelevant to nonobviousness of claim 19.

  “at the time that Gilenya was introduced, it was the first oral multiple sclerosis medication to be approved by the FDA, and there was significant pent-up demand for such a drug. ... [But] much of the demand for Gilenya was simply the demand for an oral multiple sclerosis medication generally. Patent Owners do not identify any evidence to the contrary.”

  Also, insufficient market share and sale evidence.

  For example, sales evidence excluded a competing drug that sells more than $1 billion annually, so “is unreliable as evidence that Gilenya’s sales are significant in relation to the relevant market as a whole.”

  “Patent Owners have not borne the burden of production necessary to trigger Petitioners’ burden to explain Gilenya’s commercial success as due to factors extraneous to the claimed invention.”
IF IPR INSTITUTED...

Patent Owner Response (POR) must make the case.

• May require expert declaration to support assertions of patentability, but POR needs to make argument; not enough to just have evidence in expert declaration.
TIPS: OVERCOMING § 103 CHALLENGES

Try to establish no finite number of identified predictable solutions with anticipated success.

For well-recognized unpredictable art such as chemistry/biotechnology, still a lot of ammunition, including no “reasonable expectation of success.”
USE YOUR AMMUNITION!

- It is unacceptable to pick closest prior art in hindsight.

- Use “no lead compound” rationale to attack rejection.

- Argue no articulated reasoning for picking applied prior art out of “scope and content of the prior art.” *Graham v. John Deere.*
ARGUING NO PRIMA FACIE CASE OF OBVIOUSNESS

- No reasonable expectation of success.
- Lack of predictability (i.e. invention not “predictable”).
- Teaching away.
- Prior art may support lack of predictability argument(s) and teaching away arguments.
- Consider level of ordinary skill in art evidence; what was the direction of the art as a whole?
- Consider arguing missing claim limitations.
Unpredictability can be important: show that invention was not predictable.

- Show no reasonable expectation of success.
- Show there was not a “finite number of identified, predictable solutions.”
- Show unexpected results.
- Other objective indicia of nonobviousness?

Show teaching away, particularly in so-called predictable results.

Showing lack of predictability or expectation of success may require submitting data and/or declarations earlier in prosecution; evidence to destroy, not rebut, the prima facie case.

Interview Examiner!
THANK YOU!

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