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Is obviousness becoming the new anticipation? The Federal Circuit's new paradigm in reviewing prior art

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Anticipation/obviousness

In *In re Montgomery* (Fed. Cir. 2012), the court addressed the question of whether prior art merely proposing a therapeutic method is sufficient to inherently anticipate such method.

The claim at issue recited "A method ***for the treatment or prevention of stroke or its recurrence***" comprising administering a rennin-angiotensin system ("RAS") inhibitor:

1. "to a patient ***diagnosed as in need of [stroke] treatment or prevention***,"
2. where such administration is "***for the treatment or prevention of stroke or its recurrence***."

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Anticipation/obviousness

The prior art "proposed" administering ramipril to prevent:

1. myocardial infarction;
2. stroke; or
3. cardiovascular death;

The only actual administration of ramipril reported in the reference used a dose of ramipril below the therapeutic dose as part of an initial patient "randomization" carried out before the actual trial.

- The study ultimately found that patients receiving ramipril had a statistically significant reduction in the risk of stroke, but such results were not published until after Montgomery's priority date;

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Concluding that "administering ramipril to stroke-prone patients inevitably treats or prevents stroke," the court held that the prior art's proposed protocol for ramipril administration to stroke-prone patients inherently anticipated the claims;

In response to applicant's argument that inherent anticipation requires that the claimed method have been actually performed, the court referred to its earlier *Schering* case which held that:

"[A]nticipation 'requires only an enabling disclosure,' not 'actual creation or reduction to practice.'"

In *Schering,* the court held that prior art to the compound loratidine inherently anticipated a later claim to its metabolite.

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Anticipation/obviousness

So is this new law or merely proper application of precedent by the court?

This seems to be new law.

- In both *Cruciferous* and *King* (cited by the majority), applicant merely observed a result of a process already being carried out whereas here, no one was already administering ramipril to a population that suffered from stroke or was diagnosed as prone to stroke;
- Even *Schering* related to a case where the prior art loratidine was already known to be an effective therapeutic, so its therapeutic was arguably enabled;

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This also seems to be inconsistent with Judge Dyk's earlier ruling in *In re '318 Litigation*, involving a method of treating Alzheimer's;

In re Montgomery	*In re '318*
"[E]ven if HOPE merely proposed the administration of ramipril for treatment or prevention of stroke (without actually doing so), it would still anticipate…. anticipation 'requires only an enabling disclosure,' not 'actual creation or reduction to practice.'"	[T]he specification …does no more than state a hypothesis and propose testing to determine the accuracy of that hypothesis. That is not sufficient. …If mere plausibility were the test for enablement…applicants could obtain patent rights to 'inventions' consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the 'inventor' would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis."(citing *Rasmusson*).

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Anticipation/obviousness

Judge Lourie dissented:

[A] mere description of a process that, *if* it had been carried out, *might* yield a particular *undisclosed* result is not an inherent anticipation of that result….[I]nherency requires description of action that inevitably produces a result, not merely description of action that might have been carried out, but was not, and might have yielded a particular result, but did not.

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Anticipation/obviousness

In *Eurand v. Mylan* (Fed. Cir. 2012), the court reviewed the validity of Cephalon's claims directed to (1) a modified-release dosage form the skeletal muscle relaxant AMRIX (cyclobenzaprine hydrochloride) and (2) a method of relieving muscle spasms with the formulation.

The question was whether the claimed extended release formulations and methods were obvious over the prior art immediate release formulations.

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Based on the known pharmacokinetics of the drug (Tmax, Cmax and AUC), the district court concluded that it would have been obvious to formulate a therapeutically effected extended release formulation;

it would have been obvious to a person having ordinary skill in the art to target extended-release PK values "mirroring"—in other words, bioequivalent to—those of the immediate-release cyclobenzaprine formulation.

The Federal Circuit disagreed, holding that the district court treated bioequivalence as the end of its inquiry without considering the claimed ***therapeutic effectiveness***, and whether it would have been obvious to one of ordinary skill in the art at the time of the invention that a bioequivalent PK value would satisfy that limitation.

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Anticipation/obviousness

Are *In re Montgomery* and *Eurand v. Mylan* reconcilable?

It is hard to conclude that it was less predictable in *Eurand* that the extended release formulation would work based on the PK data than it was in *Montgomery* that a proposal to treat stroke would work.

Montgomery was hurt by the fact that the court viewed Montgomery's disclosure as being no better than the prior art itself, noting that Montgomery "does not disclose actual results from the administration of ramipril for these purposes [treatment or prevention of stroke]."

Defendant's in *Eurand* raised the same issue that Eurand had not proven therapeutic efficacy any more than the prior art did, but the court concluded that "we must accept as true that cyclobenzaprine lacked a known PK/PD relationship at the time of invention, and that the asserted claims contain a valid "therapeutically effective" limitation."

Anticipation/obviousness

In *ClearValue, Inc. v. Pearl River Polymers, Inc.* (Fed. Cir. 2012), the court reviewed whether ClearValue's claim was anticipated.

The claim recites:

- A process for clarification of water of:
- ***raw alkalinity less than or equal to 50 ppm***
- by chemical treatment, said process comprising adding [polymer] in an amount sufficient to form a flocculated suspension in the water and to remove turbidity from the water….

The district court found that the prior art taught away from treating water of alkalinity of less than or equal to 50 ppm and thus confirmed the validity of the patent.

Anticipation/obviousness

ClearValue argued that the prior art's disclosure of clarifying water with alkalinity of 150 ppm or less is too broad to anticipate the 50 ppm limitation of the claim citing *Atofina*:

In *Atofina*, the court found that a patent claiming a method of synthesizing difluoromethane at a temperature between 330-450 °C. was patentable over prior art showing a broad temperature range of 100-500

- "Given the considerable difference between the claimed range and the range in the prior art" "no reasonable fact finder could conclude that the prior art describes the claimed range with sufficient specificity to anticipate this limitation of the claim."

Anticipation/obviousness

The court distinguished *Atofina*, noting that:

- "[I]n *Atofina*, the evidence showed that one of ordinary skill would have expected the synthesis process to operate differently outside the claimed temperature range, which the patentee described as 'critical' to enable the process to operate effectively."
- By contrast, "ClearValue ***has not argued*** that the 50 ppm limitation in claim 1 is 'critical,' or that the claimed method works differently at different points within the prior art range of 150 ppm or less.
- Nor does ClearValue argue that the Hassick reference fails to teach one of ordinary skill in the art how to use the claimed invention."

Anticipation/obviousness

So is this new law or merely proper application of precedent by the court?

- *Atofina* said nothing about Atofina's process operating differently from the prior art process when outside Atofina's claimed temperature range
  - Nor does such an analysis make sense because if there is true anticipation, then criticality of results is irrelevant for the very reason that if it's anticipation, the results are inherent;
- To add insult to injury, ClearValue's specification actually did allege criticality for the under 50 ppm limitation in its specification
  - This probably explains why the court held that "ClearValue has not argued that the 50 ppm limitation" is critical.

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Anticipation/obviousness

In *Wrigley v. Cadbury* (Fed. Cir. 2012):

Wrigley claimed a gum including as flavor components menthol and a N-2,3-trimethyl-2-isopropyl butanamide ("WS-23");

The district court concluded that the gum was anticipated by prior art disclosing both components among a large list of components;

The prior art did not disclose or exemplify the specific combination;

On appeal, Wrigley argued that (1) while the prior art discloses all the claim limitations, it does not disclose them in the combination recited; and (2) the prior art would not have enabled a person of ordinary skill in the art to derive the claimed combination without undue experimentation.

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Anticipation/obviousness

The prior art disclosed an oral dental composition:

- in the form of toothpastes, mouth rinses, liquid dentifrices, lozenges and gums
- including as essential components xylitol, copper bis-glycinate and a pharmaceutically acceptable carrier;
- and as optional components:

(1) water; (2) **cooling agents including WS-23**, WS-3 and TK-10; (3) a water-soluble fluoride agent; (4) a humectant; (5) an abrasive polishing material; (6) a surfactant; (7) stannous salts; (8) non-cationic water insoluble agents; (9) **flavoring agents** including, among a list of twenty four, **menthol**, and (10) five other optional components.

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Anticipation/obviousness

So in order to arrive at the claimed combination, one of ordinary skill in the art had to take the following steps:

1. select a gum from among the five oral dental compositions (1/5);
2. Use one of the optional components (1/2);
3. Use a cooling agent as one of the optional components (1/14)
4. Use WS-23 as the cooling agent (1/3)
5. Use a flavoring agent (1/14);
6. Use menthol as the flavoring agent (1/24)

This is a selection involving one of over 160,000 choices!

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Anticipation/obviousness

The Federal Circuit held that:

- "[T]he number of categories and components in Shahidi" was not "so large that the combination of W-23 and menthol would not be immediately apparent to one of ordinary skill in the art."
- "Shahidi envisions using WS-23 and menthol in a single product."
- "While Shahidi discloses a number of different combinations of cooling and flavoring elements, one of them is the combination of menthol, which Shahidi identifies as one of the 'most suitable' flavoring agents, with WS-23, which Shahidi identifies along with WS-3 as among a group of three 'particularly preferred cooling agents.'"
- "Based on the disclosure of the combination of those components, we agree with the district court that Shahidi anticipates [the claim]."

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Anticipation/obviousness

So is this new law or merely proper application of precedent by the court?

Selecting specific combinations of components, where each component itself has to be selected from a separate list of optional components, has generally not been viewed as anticipatory.

See Akzo v. US ITC holding no anticipation where the prior art "would have required [patentee] randomly to pick and choose among a number of different polyamides, a plurality of solvents, and a range of inherent viscosities.")

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Anticipation/obviousness

So is this new law or merely proper application of precedent by the court?

Note that the court also seemed to rely on Wrigley's own disclosure as a roadmap to find anticipation:

"***Given the objective of the [Wrigley] patent***, to obtain 'a cooling flavor composition that will contribute a long-lasting cooling sensation' and a chewing gum with a 'clean, high-quality flavor … with a good cooling effect,' the Shahidi reference clearly identifies the combination of WS-23 … and menthol."

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Anticipation/obviousness

Is this decision right?

Judge Newman dissented:

- "This court has explained that, in order to anticipate, the prior art must be such that a person of ordinary skill would 'at once envisage' the specific claimed composition….When the listing of many possible ingredients does not produce immediate recognition of the specific combination, the list does not anticipate the combination."

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Anticipation/obviousness

In *Santarus, Inc. v. Par Pharmaceutical, Inc.* (Fed. Cir. 2012), the court reviewed claims to specific combinations of the uncoated benzimidazole PPI and buffering agents administered orally as a single dose of an aqueous solution or a suspension.

The prior art disclosed formulating omeprazole both in conventional dosage forms (e.g., tablets, capsules, and granules) and also as an aqueous suspension of omeprazole with a buffering agent.

- An example disclosed a suspension formed by mixing enteric coated omeprazole with water/sodium bicarbonate solution;
- The prior art also taught that the omeprazole does not need to be enterically coated and that even the coated drug could be formulated into a suspension which breaks down the coating.

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Anticipation/obviousness

Santarus argued that that at least some of the claims recite a specific blood serum concentration levels not disclosed in the prior art;

The court disagreed, holding that "The initial blood serum concentration resulting from administering a PPI dosage is an inherent property of the formulation, and an obvious formulation cannot become nonobvious simply by administering it to a patient and claiming the resulting serum concentrations."

- To hold otherwise would allow any formulation – no matter how obvious – to become patentable merely by testing and claiming an inherent property.
- There is no dispute that the blood serum concentrations claimed are expected in light of the dosages.

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Anticipation/obviousness

The court reviewed a second set of claims which were entitled to an earlier priority date over different prior art.

Santarus contended that the prior art "ruled out" non-enteric coated tablets, capsules, and granules and thus discouraged a skilled artisan from using any non-enteric coated oral dosage forms of PPIs.

- The court agreed that the prior art explicitly "ruled out" non-enteric coated conventional oral dosage forms because they degrade too quickly in the stomach to be absorbed in sufficient amounts to be effective and thus teaches away from such formulations.
- However, for the claims covering powder formulations for use in aqueous suspensions, the court found no teaching away in view of prior art teaching that uncoated formulations containing a buffer could be used as an alternative to enteric coating in order to protect omeprazole from degrading in the stomach

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Anticipation/obviousness

Finally, the court found claims requiring far lower amounts of buffering agent than disclosed in the prior art to be non-obvious.

The court rejected Par's argument that it was sufficient that the prior art disclosed the claimed ratio of sodium bicarbonate to PPI such that it would have been obvious to reduce the total amount of buffer disclosed in those references so long as the amount of drug was also reduced.

–Par points to nothing in the prior art that indicates it was the ratio of buffering agent to PPI, as opposed to the total amount of buffer consumed, that was the key to preventing the stomach from being too acidic.

–Given the prior art's teachings regarding protecting omeprazole from stomach acid, it would not have been obvious to decrease the amount of sodium bicarbonate disclosed in the prior art.

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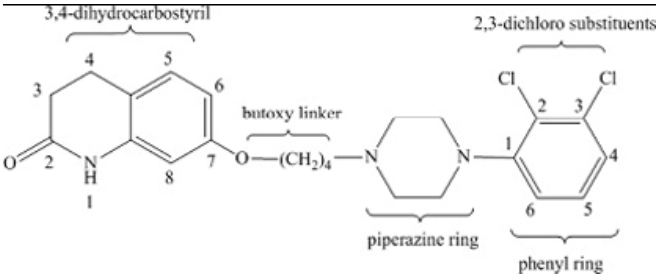
Anticipation/obviousness

In *Otsuka Pharma v. Sandoz* (Fed. Cir. 2012), the court reviewed the validity of ABILIFY, an antischizophrenic drug



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Anticipation/obviousness

Defendants proposed the structurally closest "carbostyril" compounds as the lead compounds for assessing obviousness;

Otsuka argued that structurally more remote compounds, clozapine and risperidone, were the "natural and obvious" structures one would have considered to modify to obtain improved antipsychotic compounds because they were the only marketed antipsychotic compounds at the time of the invention.

The Federal Circuit agreed with Otsuka that carbostyrils were not "plausible lead compounds" because at the relevant time there were no carbostyril compounds that (1) were marketed as antipsychotics or (2) were publicly known to have potent antipsychotic activity with minimal side effects.

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Anticipation/obviousness

The court rejected the unsubstituted butoxy compound (differing from the claimed compound in that it lacks two chloros on the phenyl ring) as a lead compound.

Although not specifically disclosed as an antispychotic, the unsubstituted butoxy was specifically disclosed as an antihistimine.

The court held that "one of ordinary skill would [not] have selected the prior art unsubstituted butoxy compound as a lead compound for further antipsychotic research."

Question: For a compound claim, is it necessary for the lead compound to have antipsychotic activity if it possesses other activities? See In re Dillon.

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Anticipation/obviousness

The court also rejected the 2,3-dichloro propoxy compound (differing from the claimed compound by employing a propoxy linker rather than a butoxy linker) as a lead compound;

The prior art lists the 2,3-dichloro propoxy compound as one among hundreds of examples that may be useful for an extensive list of potential central nervous system controlling activities, and fails to tie the compound to any meaningful suggestion of antipsychotic activity.

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Anticipation/obviousness

The court also rejected the OPC-4392 (differing from the claimed compound by including a propoxy rather than butoxy linker and by including two methyl groups rather than two chloro groups on one of the rings) as a lead compound;

The totality of the evidence shows that the compound was considered a failure insofar as it did not treat the positive symptoms of schizophrenia and was not well-tolerated in modest doses.

Anticipation/obviousness

Finally, the court held that the claimed dichloro compound was not invalid for obviousness-type double patenting over the prior art compound with an unsubstituted phenyl ring:

The evidence demonstrates a high degree of unpredictability in antipsychotic drug discovery;

Although 2,3-dichloro substituted compounds disclosed in the prior art, that art failed to tie that disclosure to any meaningful suggestion of antipsychotic activity.

At the time of the invention, there was no known antipsychotic drug that had those two particular chlorine substituents arranged in a 2,3 orientation and no teaching suggesting that a dichlorination pattern would lead to a safe atypical antipsychotic or even an antipsychotic period, atypical or otherwise

Thank You!

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