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All Things Chemical and Biotechnical at the PTO

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ARE DIAGNOSTIC METHOD CLAIMS STILL PATENTABLE?

Case: *Prometheus Labs. v. Mayo Collaborative Services*, 581 F.3d 1336, 92 U.S.P.Q.2d (BNA) 1075 (Fed. Cir. 2009)

Discussion of the Case:

This case presents the first application of the "Bilski" test for patentable subject matter to pharma/biotech subject matter.

Facts of the Case:

Prometheus is the exclusive licensee of US Patents 6,355,623 and 6,680,302 at issue, which claim methods for treating autoimmune diseases, including gastrointestinal AI diseases such as inflammatory bowel disease and Crohn's disease by administration of thiopurine drugs. The thiopurines include 6-mercaptopurine and azathiopurine, a pro-drug of 6-MP. 6-MP is broken down by patient metabolism to many metabolites. Thiopurine treatment must be carefully monitored so that an effective, but non-toxic dose is maintained.

Claim 1 of the '623 patent is representative of the claims at issue:

A method for optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:

- (a) administering a drug providing 6-thioguanine to a subject having said immune-related gastrointestinal disorder; and
- (b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder,

Wherein the level of 6-thioguanine less than about $230 \text{ pmol per } 8 \times 10^8$ red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and

Wherein the level of 6-thioguanine more than about $400 \text{ pmol per } 8 \times 10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

Prometheus sued Mayo for infringement of the '623 and '302 patents. The District Court granted Mayo's motion for summary judgment that the asserted claims 1, 7, 22, 25 and 46 of the 623 patent and claim 1 of the '302 patent were invalid under 35 USC § 101 as being directed to non-statutory subject matter. The District Court reasoned that the claims included three steps - administering a drug to a subject, determining metabolite

levels, and warning that an adjustment of dosage may be required. The District Court took a position that the administration and determination steps were "mere data gathering" and that the "warning" step was only a mental step based upon a natural relationship that the inventors had merely observed.

The District Court found that correlations [between particular concentration of 6-TG and 6-MMP and therapeutic efficacy and toxicity] were natural phenomena not invented by the Inventors. The District Court also found that, because the claims cover the correlations themselves, the claims "wholly pre-empt" the correlations.

On Appeal:

Review of a decision on summary judgment is *de novo*, and review of a question presented under 35 U.S.C. § 101 is a question of law also reviewed *de novo*.

Judge Lourie wrote for the Federal Circuit.

The CAFC applied the "machine or transformation" test set forth in *In re Bilski*, 545 F.3d 943, 88 U.S.P.Q.2d 1385 (Fed. Cir. 2009), and described as "definitive" in the *Prometheus* opinion. It appears that by "definitive" the Court means that a claim passing the test is "surely patent-eligible subject matter," not that it is the only test for patent-eligibility.

The "machine or transformation" test is articulated as, "a claimed process is surely patent-eligible under § 101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing." (citing *Bilski*) Note that the test is one of meeting either alternative.

Furthermore, such claim elements as relate to the machine or transformation must represent more than "insignificant extra-solution (from an algorithm or natural process) activity" or "mere data gathering" and must be "central" to the claimed subject matter. Finally, the inclusion in the claimed process of steps of a mere algorithmic character will not invalidate a claim that includes other steps that meet the machine or transformation test. The Court emphasized that the *Bilski* Court had determined that *In re Abele*, 684 F.2d 209, 214 USPQ 682 (CCPA 1982) remained good law. In *Abele* a claim utilizing an algorithm to process CAT scan data was found patent-eligible, because once the algorithm-reciting steps were removed from the claim, there remained steps for performing the CAT scan. (That is, *Abele* might be viewed as an instance where the claim passes the "machine" test.)

Applying these rules to *Prometheus*' claims, the Court found that the step of "administering a drug" constituted a transformation of a human body, and that the metabolism of the drug was a transformation of an article; either being sufficient to establish patent-eligibility. The Court also found that, since the claim was directed to a "method of treatment", **as made clear in the specification and the preambles of**

the asserted claims, this step was central to the claimed subject matter and therefore Prometheus' claims were patent-eligible subject matter.

Interestingly, the Court also found that the step of "determining the level of 6-thioguanine..." was also a sufficient transformation. Here the Court simply stated that:

Determining levels of 6-TG or 6-MMP in a subject **necessarily** involves a transformation, for those levels cannot be determined by mere inspection. Some form of manipulation, such as the high pressure liquid chromatography method specified in several of the asserted dependent claims or other modification of the substances to be measured, is necessary to extract the metabolites from a bodily sample and determine their concentrations. **As stated by Prometheus' expert**, "at the end of the process, the human blood sample is no longer human blood, human tissue is no longer human tissue."

92 U.S.P.Q.2d at 1081 (emphasis added).

The Federal Circuit decided that the District Court had made two errors. First, the District Court erred in finding that the "determining" steps were merely data gathering. The Federal Circuit reasoned that, although true that the determining steps gather useful data, they are also a part of the protocol for the claimed method of treatment; the measurement of the level of the drug metabolite levels was used for the purpose of determining the dosage of the drug to be administered. Second, the District Court erred in deciding that the claims covered the correlations themselves, and thus "wholly pre-empted" all uses of the correlations. Since the claim as a whole was found "transformative" it did **not** "wholly pre-empt" all uses of the correlations. Thus, on this second question, the District Court used the correct standard ("wholly pre-emptive"), but applied it incorrectly.

Accordingly, the decision of the District Court that the claims asserted by Prometheus were invalid under 35 U.S.C. § 101 as directed to subject matter that is not patent eligible was reversed, and the case was remanded to the District Court for further proceedings.

Practice Tip:

The decision makes it pretty clear that "method of treatment" claims remain patent-eligible subject matter after *Bilski*, since any such claim would recite a step of "administering" a compound to a subject, thus "transforming" the subject. It does behoove the practitioner to make clear that the claim is directed to a method of treatment by describing that in the preamble of the claim.

Less clear is the fate of claims to "diagnostics". Plainly a claim reciting steps utilizing a particular method of measurement would remain patent-eligible, since "transformations" of the sample or use of a particular machine would be described in the

claim. However, nothing in the decision clearly establishes that a claim broadly written as a step of determining a level of a substance in a sample and making a diagnostic decision based upon the result includes a sufficient "transformation". There is, though, the Court's statement that a step of determining the level of a substance in a sample is "necessarily" transformative, because such levels are not determinable by mere inspection, which suggests that when presented with this question the Court would find such claims patent-eligible. The Court relied on expert testimony on this point, and so it may be necessary to obtain such testimony in the instance of litigation of a claim to a diagnostic method broadly written to recite only the basic correlation elements. Again, a "method of diagnosis of disease X" should be recited in the preamble of the claim, so that the "determining" step may be found central to the purpose of the invention.

IS SPECULATION REGARDING UTILITY SUFFICIENT?

Case: *Amgen, Inc. (09/895,943) v. Human Genome Sciences Inc. and Schering Corp. (6,844,170)*, Patent Interference No. 105,613, 2009 Pat. App. LEXIS 12 (BPAI June 5, 2009)

Discussion of the Case:

The styled case is an "informative" decision on a HGS' petition for rehearing of the Board's decision to enter judgment based on a finding that the claims of HGS' US Patent 6,844,170 were invalid for lack of substantial, specific utility. HGS also sought consideration of a motion for judgment based on priority and that Amgen's claims were invalid under 35 U.S.C. §§ 102(e)/103. HGS' petition was denied.

Our interest in this case is with respect to the decision about utility. The relevant paper is paper 74 in the interference, Decision – Bd.R. 125 – On Motions. Majority opinion by Torczon. Tierney writes a concurring opinion, and Gardner Lane dissents.

Facts of the case

Claim 15 of the '170 patent was deemed representative and also defines Count 1 of the interference:

An isolated polynucleotide consisting of a nucleic acid encoding a fragment of SEQ ID NO:2, wherein said fragment is at least 30 contiguous amino acid residues in length and wherein said fragment can be used to generate or select for an antibody that specifically binds the polypeptide of SEQ ID NO:2.

SEQ ID NO: 2 is the amino acid sequence of a particular receptor "CRCGCL".

At issue was whether HGS' US Patent 6,844,170 was supported by disclosure of a specific, substantial and credible utility for the involved claims. The Board indicates that a finding of sufficient utility for the protein fragment, or of the antibodies it can be used to raise, would be sufficient to confer utility to the polynucleotide encoding the fragment.

The Board adopts Amgen's assertion of nearly 300 medical utilities by the '170 patent and explains that the disclosure provided by HGS' disclosure is prophetic, there being no actual demonstration of any of them, or are purely speculative, being suggested by analogy to the function of other proteins based on sequence homology. The Board provides the following sample of the disclosure of utility in the '170 patent:

The tissue distribution of [the CRCGCL] gene in cells of the immune system suggests that the protein product of this clone would be useful for treatment, prophylaxis and diagnosis of immune and autoimmune diseases, such as lupus, transplant

rejection, allergic reactions, arthritis, asthma, immunodeficiency diseases, leukemia, AIDS. In addition its expression in T-cells suggests a potential role in the treatment, prophylaxis and detection of thymus disorders such as Graves [d]isease, lymphocytic thyroiditis, hyperthyroidism and hypothyroidism. The receptor could also serve as a target for small molecule or monoclonal antibody, blocking its activity, which could be important in the disease states listed herein.

Other disclosed uses for the polynucleotide include the use of— variant polynucleotides for optimizing protein production in different host organisms;
polynucleotide fragments as probes or primers;
polynucleotides in gene therapy;
polynucleotides for identification of individuals;
polynucleotides as hybridization probes for differential identification of tissues or cells;
polynucleotides for gene expression level assays; and
polynucleotides as molecular weight markers.

In the course of the interference, HGS chose to assert most strongly a utility of differential identification of activated vs. resting T-cells.

The HGS specification discloses that SEQ ID NO:2 (the polypeptide sequence used to define the claimed polynucleotides) was deduced from the sequence of a clone isolated from an activated T-cell cDNA library. The nature and source of the activated T cells comprising the library is not disclosed. An assay for expressed polynucleotides is disclosed and many cell types are surveyed, including activated T-cells and Molt-4 cells, an immortalized T-cell line. The specification proceeds to suggest that because CRCGCL was isolated from activated T cells, nucleic acids of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of immune disorders. The specification also states that because CRCGCL is found expressed in a cervical cancer cell line (HeLa), activated T cells, and a lung carcinoma cell line (A549), while a shorter variant is also expressed in the lymph node and to a lesser extent in the spleen, CRCGCL polynucleotides are useful as hybridization probes for differential identification of the tissue(s) or cell type(s) present in a biological sample.

Amgen provided expert testimony that, "one of skill reading the HGS application when it was filed would have thought the listed utilities fell below the substantial, specific and credible threshold," and that a skilled artisan would have been skeptical of inferences HGS drew based upon sequence homology. The testimony of Amgen's expert (Dr. Ziegler) established that the skilled artisan would not have taken any lesson from the disclosure that could be specifically applied to a fragment of CRCGCL protein:

In addition, the assertion that nucleotides for CRCGCL may be

useful for “differential identification” of tissue or cells in a biological sample is also the case for virtually any polypeptide, and provides the person of ordinary skill no information regarding a utility specific to CRCGCL.

The parties both presented post-filing evidence to support their positions on utility. The Board was unwilling to consider testimony evidence presented by Amgen that one of ordinary skill in the art would have understood the differential identification of resting vs. activated T cells from the specification, explaining that the Declarant did not tie his conclusions to specific disclosure in the specification.

On the other hand, the Board relied strongly upon publication evidence presented by Amgen that showed that HGS had likely mis-identified SEQ ID NO: 2 as GRCGCL; instead the protein appears to be a TSLPR gene. Although belonging to the same gene family, the TSLPR and GRCGCL genes have different expression profiles among myeloid and lymphoid cells, and that differential expression of TSLPR in resting vs. activated T cells is slight.

The Decision provides a review of the standards for utility, rejecting a notion (raised by the dissent) that mere nominal utility is sufficient and re-stating a need for a specific, substantial and credible utility. There is a requirement that one casting doubt on an asserted utility must establish a *prima facie* case of lack of utility, and the Board found that Amgen met this requirement by their evidence of unpredictability in the art and of HGS’ misidentification of SEQ ID NO: 2.

The Board gives us a review of the allowed uses of post-filed evidence. The Board starts from a case holding that post-filing evidence cannot be used to show appreciation of operability of the invention for its intended use to establish actual reduction to practice in an interference. Extending that holding, the Board seems to say that post-filing evidence cannot be used to ascertain the state of mind of the inventors at filing, and thus cannot be used to address a question of specificity of utility. However, such evidence is admissible on the question of substantiality and credibility of a clearly asserted utility, perhaps especially so when used to cast doubt upon an assertion of utility.

The Board then proceeds to address the three requirements for utility. The Board found a lack of substantial utility, first in that the precise utility of distinguishing between activated and resting T cells was not expressly disclosed. The disclosure that the polynucleotide of the invention could be used as a marker to distinguish cells in which [the GRCGCL] gene is expressed from those in which it is not expressed was deemed “a biotechnological tautology” and that such disclosure of differential expression as was provided was merely a suggestion for further research. Thus, there was not sufficient disclosure to make "differential T-cell identification presently available."

The Board also found a lack of specific utility. Referring to the tautological disclosure noted above, the Board pointed out that, "[i]f this were a well-established and

particularly beneficial utility, then any isolated gene, regardless of biological function, has a specific utility as a research tool."

As to credibility, the Board notes that if the test is mere facial possibility, then HGS' asserted utility passes it. However, the Board suggests that the question is more whether a skilled artisan reading HGS' disclosure would believe that they could make the invention work.

Finally, addressing the question of selection of an operable utility from among a list of others that fail or are untried, the Board suggested that the statement of a long list of speculative uses having little actual support was itself evidence of lack of a specific, substantial utility.

The Concurrence and Dissent

The concurring and dissenting opinions show the use of the threshold for utility as a tool to adjust policy. The Concurrence suggests that it is inappropriate to grant patents of wide scope based upon limited, speculative disclosure of utility, where the applicant is "just guessing" about use to which the invention may be put. "Utility must be apparent from the specification itself at the time of filing." It is insufficient to put the public in the position of having to discern a substantial, specific and credible utility the inventor intended to contribute to the progress of the useful arts "from among all of the other faint and false trails disclosed."

The Concurrence properly notes an enablement component to the social contract of a patent,

HGS cannot be rewarded for educated speculation based on homology and some very preliminary results. HGS did not demonstrate in its specification any practical utility capable of immediate real-world application. The large number of possible utilities in the specification made the amount of experimentation necessary to determine which might be useful so onerous that it was an unreasonable, even if much of it would have been routine.

So, § 101 is a blunt instrument; all scope of claims is denied unless at least one immediately practical benefit of the invention is expressly disclosed.

On the other hand, the Dissent argues that the case law establishes that the threshold for utility is "low", and asserts that the disclosure deemed "tautological" by the majority is sufficient:

The qualms of the majority are understandable. Any naturally occurring polynucleotide or polypeptide, or any antibody to the polypeptide, can be used as a marker, even if additional markers are necessary for effective identification. Thus, all naturally occurring

polynucleotides or polypeptides are *prima facie* useful the minute they are isolated from a known source. For better or worse, precedent requires a finding of utility in this circumstance.

The Dissent also places much faith in the abilities of the artisan skilled in molecular biology, and so believes that Amgen failed to meet their burden on *prima facie* lack of utility...

Although HGS does not give a specific example of CRCGCL being used to differentially identify activated T cells in a heterogeneous tissue or cell sample, the level of skill in this art is so high that, if the method works at all, those in the art could quickly determine that fact. No one provided test results that indicate whether differential identification performed using CRCGCL as described in the HGS specification would or would not work. Thus, we are left with the presumption that the claimed invention does what it is described to do.

Practice Tip:

If you are looking for an attack on validity, review the specification to see if it discloses a number of general utilities and whether there is any disclosure of a utility that is particular to the claimed subject matter as keys to an attack based upon lack of substantial, specific utility.

If you are drafting, press inventors to discuss the most likely utility in detail. If you are saddled with a general disclosure, place an application on file that includes disclosure of a utility particular to the claimed, elected subject matter as soon as that disclosure is available from the research project.

If you are prosecuting, the Examiner must first make a *prima facie* case of lack of utility. You may have to answer with evidence of how the skilled artisan can understand the asserted utility from the written disclosure. Declaration testimony should tie its conclusions to specific passages from the specification (and originally-filed claims and drawings). Declarants are preferably available for deposition later, otherwise a new Declarant on the same points might be required in a later validity contest.

WHEN ARE PROPHEPIC EXAMPLES SUFFICIENT?

Case: *Ariad v. Lilly*, 560 F.3d 1366, 90 U.S.P.Q.2d (BNA) 1549 (Fed. Cir. 2009)

Discussion of the Case:

The claims at issue in this case deal with a method for regulation of a transcription factor, which is a molecule found in cells that regulates the extent to which genes are expressed. Inventors of U.S. Patent No. 6,410,516 (the '516 patent) discovered a transcription factor that they named NF-KB. The four claims of the '516 patent at issue address a method of reducing NF-KB activity such that gene expression is reduced, thereby causing the cell to produce fewer corresponding proteins, which are harmful in excess.

Ariad sued Lilly for infringement of the four claims. Lilly asserted that the claims were not infringed and were invalid on grounds of anticipation, lack of enablement and lack of written description. Those issues were addressed during a jury trial; the jury found infringement of all four claims and concluded that the claims were not invalid for anticipation, lack of enablement or lack of written description. Further, a bench trial addressed Lilly's defenses that the claims were directed toward unpatentable subject matter and unenforceable due to inequitable conduct or prosecution laches. The court found the asserted claims patentable and not unenforceable.

On appeal the Federal Circuit addressed two issues, (1) whether the claims were invalid for lack of written description under 35 U.S.C. §112 and (2) whether the claims were unenforceable due to inequitable conduct.

First, as to the written description requirement, the court emphasized the language of 35 U.S.C. §112 which states: "[t]he specification shall contain a written description of the invention." Following *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005) and *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 922 (Fed. Cir. 2004), the court explained that the requirement ensures meaningful disclosure of the patent and the scope of the right to exclude, and it demonstrates the patentee's possession of the invention claimed. No particular form of disclosure is required; however, the written description of the patent in the specification should demonstrate possession of the invention with 'reasonable clarity'. The court stated that, for both process and composition claims, "where the specification provides only constructive examples in lieu of working examples, it must still 'describe the claimed subject matter in terms that establish the applicant was in possession of the claimed invention, including all of the elements and limitations.'" *quoting Rochester*, 358 F.3d at 926.

Satisfaction of the written description requirement is a fact-based inquiry that depends on the nature and context of the claimed invention. The following factors were addressed to evaluate the adequacy of the written description: (1) "existing knowledge in the particular field," (2) "extent and content of the prior art," (3) "maturity of the science and technology," and (4) "predictability of the aspect at issue." *quoting Capon*, 418 F.3d

at 1359. In this case, it was undisputed that the claimed invention "was made in a new and unpredictable field where the existing knowledge and prior art was scant."

Lilly argued that the written description was inadequate because the specification fails to disclose how the claimed reduction in NF-KB is achieved. Both parties agree that the specification does hypothesize that three classes of molecules are potentially capable of reducing NF-KB activity: specific inhibitors, dominantly interfering molecules, and decoy molecules. Ariad claimed that because it did not actually claim the molecules, it could claim the methods without describing the molecules. Lilly argued that the hypothesis in the specification is "little more than a research plan" and thus inadequate.

Following *Rochester*, the court held that:

[r]egardless of whether the asserted claims recite a compound, Ariad still must describe some way of performing the claimed methods, and Ariad admits that the specification suggests only the use of the three classes of molecules to achieve NF-KB reduction. Thus, to satisfy the written description requirement for the asserted claims, the specification must demonstrate that Ariad possessed the claimed methods by sufficiently disclosing molecules capable of reducing NF-KB activity...

The court looked to the description of each class of molecule in the specification to determine whether Ariad had sufficiently disclosed molecules capable of the claimed method. The court found: only "a vague functional description and an invitation for further research" of the first class of specific inhibitors; "no example" of dominantly interfering molecules and only a "plan for further research"; and example structures of decoy molecules without adequate description of the use of those molecules to reduce NF-KB activity.

Specifically, with regard to the decoy molecules, the full extent of the specification's disclosure was that "NF-KB 'would bind the decoy' and thereby, 'negative regulation can be effected.'" The court stated that "[p]rophetic examples are routinely used in the chemical arts, and they certainly can be sufficient to satisfy the written description requirement." However, in this case, the court found the disclosure to be a "mere mention of a desired outcome," with "no descriptive link between the table of decoy molecules and reducing NF-KB activity." Therefore, because no working or prophetic examples of the claimed methods, or molecules capable of the claimed methods, were disclosed, the court held the claims invalid for lack of written description.

With regard to the issue of inequitable conduct, the court found that Lilly did not establish a threshold level of intent to deceive by clear and convincing evidence. The court held, "materiality and intent are different requirements, and absent a finding of deceptive intent, no amount of materiality gives the district court discretion to find inequitable conduct." Therefore, the court affirmed the ruling that the patents were not unenforceable due to inequitable conduct.

Concurrence: Judge Linn

Judge Linn expressed concern that the court is reading a separate written description requirement into the statute. Judge Linn stated that the statute "requires no more of the specification than a disclosure that is sufficient to enable a person having ordinary skill in the art to make and use the invention." In other words, the written description is part of the enablement requirement, and the sufficiency of the disclosure should be based on whether it enables a person skilled in the art to make or use the invention and sets forth the best mode.

In this case, because the court relied solely on the written description requirement for a finding of invalidity, it did not address Lilly's argument of lack of enablement, which would have required the court to address the important issue of whether broad claims that "cover any method for achieving a particular result" meet the enablement requirement.

Rehearing:

On August 21, 2009, the court granted a rehearing *en banc* to determine (1) whether 35 U.S.C. §112, paragraph 1, contains a written description requirement separate from an enablement requirement, and (2) if there is a separate written description requirement, what is its scope and purpose.

Practice Tip:

Practitioners need to watch this case carefully. If the basic holding of this case remains intact after the en banc review, some applicants might decide to delay filing of a patent application on inventions where the utility has not yet been demonstrated by experimental work or where the utility cannot be easily inferred from the teachings of the specification. This case could have a significant impact on companies doing basic research in the medical field and universities that might have enough funding for a project to do the additional tests necessary to confirm utility.

WHEN IS A DNA SEQUENCE NEW?

Case: *In re Gleave*, 560 F.3d 1331, 90 U.S.P.Q.2d (BNA) 1235 (Fed. Cir. 2009)

Discussion of the Case:

The claims at issue in *Gleave* were directed to an antisense oligodeoxynucleotide designed to bind to two different types of insulin-dependent growth factor binding protein ("IGFBP"). The claims were rejected as anticipated or obvious under 35 U.S.C. § 102(b)/103(a). The cited art disclosed more than 1,400 15-mer sense oligonucleotides that may be made from the IGFBP-2 gene. The cited art further disclosed that antisense oligonucleotides may comprise any oligonucleotide that specifically hybridizes with any of the disclosed 15-mer sense oligonucleotides.

Gleave argued that the cited art merely disclosed a list comprising "ink, formed into strings of letters" not disclosure of any functional antisense oligonucleotides. Gleave also cited *In re Wiggins*, 488 F. 2d 538 (CCPA 1973) for the proposition that a list of compounds without any direction as to selection among the targets, is not a description of any one of those targets.

The court stated that if a reference discloses all of the claim limitations and enables the subject matter that falls within the scope of the claims at issue, the reference anticipates. The court considered *Wiggins*, which found no anticipation on similar facts relating to chemical compounds since the "mere naming of a compound in a reference, without more, cannot constitute a description of the compound." However, the court stated that 'without more' is the key phrase. What is "more" is the ability to make the compounds. Chemical compounds disclosed by structure are not necessarily enabled. For Gleave's composition claims, however, the prior art reference satisfied the enablement requirement under 35 U.S.C. § 102(b) since an ordinary artisan would know how to make the described sequences. The court considered it irrelevant that the cited art did not provide an understanding of which of the targets would be useful. The court emphasized that, to satisfy the enablement requirement under 35 U.S.C. § 102(b), a reference does not need to disclose a use or a utility requirement. If the issue concerned a method claim, however, it would be largely meaningless to require a reference to disclose how to "make" that method. In effect, for method claims, the "make" requirement becomes a "use" requirement.

In conclusion, anticipatory prior art does not need to be functional, useful, or show actual reduction to practice. Rather, to be anticipatory, the prior art must enable the skilled artisan to make the claimed invention.

Practice Tip:

The court's decision suggests that nucleic acids can be anticipated by the recitation of any sequence or its complement in the prior art. Accordingly, defensive publications providing lists of sequences may be used to block others from obtaining

protection. Applicants attempting to obtain protection for sequence compositions should continue to draft patent applications with sufficient support for method claims as a back up position.

ARE DNA SEQUENCES STILL PATENTABLE?

Case: *In re Kubin*, 561 F.3d 1351, 90 U.S.P.Q.2d (BNA) 1417 (Fed. Cir. 2009)

Discussion of the Case:

In *In re Kubin*, claim 73 of the application was drawn to the following subject matter:

73. 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.

This specification of the Kubin application described that the amino acid sequence set forth in SEQ ID NO 2 the human natural killer cell activation inducing ligand ("NAIL"), which was cloned by applicants using a commercially available antibody and known cloning methods. The prior art also disclosed that the commercially available antibody used by applicants to clone NAIL recognizes a 38 kilodalton protein, later shown to be NAIL. Although the prior art did not disclose the exact amino acid sequence of NAIL or a cDNA that encodes NAIL, the prior art did disclose the exact amino acid sequence of the mouse NAIL homologue, the sequence of a cDNA molecule encoding the mouse homologue and that the mouse homologue binds CD48. The examiner found the claimed subject matter obvious over the combined teachings of the prior art.

On appeal, the USPTO Board of Patent Appeals and Interferences ("the Board") cited to KSR, and affirmed the examiner's obviousness rejection on the grounds that:

The "problem" facing those in the art was to isolate NAIL cDNA, and there is a limited number of methodologies available to do so. A skilled artisan would have had reason to try these methodologies with a reasonable expectation that at least one will be successful. Thus, isolating NAIL cDNA was "the product not of innovation but of ordinary skill and confidence," leading us to conclude NAIL cDNA is not patentable as it would have been obvious to isolate.

This Board decision was, of course, directly counter to the holdings of prior Federal Circuit cases of *In re Bell* and *In re Deuel*. Important to this decision is the fact that the Board found the state of the art had advanced significantly and become "predictable" in the 10 years following *In re Deuel*.

The CAFC affirmed the Board's decision on essentially the same grounds stated by the Board. In affirming the Board's decision, the CAFC stated:

"The record shows that the prior art teaches a protein of interest, a motivation to isolate to isolate the gene coding for that protein, and illustrative instructions to use a

monoclonal antibody specific to the protein for cloning this gene. Therefore, the claimed invention is 'the product not of innovation but of ordinary skill and common sense' (citing *KSR*).

The court noted the argument that one of the references of record suggests that the gene is not expressed in humans and therefore the prior art teaches away from the invention. However, the CAFC found that when the prior art as a whole is considered, the prior art "would have aroused a skilled artisan's curiosity to isolate the gene coding for p38." And, even though the biotechnological arts are generally considered "unpredictable", the CAFC held that in this case "one of ordinary skill in this advanced art would find these claimed 'results' [successful cloning] profoundly 'predictable'." Thus, "the claimed invention was reasonably expected in light of the prior art and 'obvious to try'" (citing *Ortho-McNeil Pharm., Inc. v. Mylan Labs. Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008)).

Practice Tip:

Many examiners at the PTO do not seem to be citing this decision in their rejections. If an examiner indicates that even very narrow DNA sequence claims that correspond to a "known gene" are allowable, it may be advisable to cancel the broader claims and obtain a patent on the narrow claims. If you do not accept the narrow claims, the examiner might change his/her mind and reject even the narrow claims. Broader claims can be pursued in a continuation application if desired.

THE "LEAD COMPOUND ANALYSIS" AND REASONABLE EXPECTATION OF SUCCESS

Case: *Procter & Gamble Co. v. Teva Pharm. USA Inc.*, 566 F.3d 989, 90 U.S.P.Q.2d 1947 (Fed. Cir. 2009)

Discussion of the Case:

Procter & Gamble (P&G) owns U. S. Patent 5,583,122 (the '122 patent) that claims the compound risedronate, the active ingredient of P&G's osteoporosis drug Actonel®. Risedronate is one member of a class of drugs known as bisphosphonates.

Teva argued that the '122 patent was obvious over P&G's own prior expired U. S. patent 4,761,406 (the '406 patent). The '406 patent lists 36 molecules as treatment candidates and 8 compounds, including 2-pyr EHDP. Teva argued that one skilled in the art would have selected 2-pyr EHDP as the lead compound and that one skilled in the art would have modified the structure of 2-pyr EHDP to arrive at risedronate.

After evaluating a number of bisphosphonates, P&G selected risedronate as the lead compound for treating osteoporosis.

On appeal, the Federal Circuit looked at several issues considered by the District Court.

Lead Compound

The court did not render a decision on the lead compound question because it found the patent valid for other reasons.

Reasonable Expectation of Success

The court held that even if 2-pyr EHDP was selected as the lead compound, "there could have been no reasonable expectation as to risedronate's success." 90 U.S.P.Q.2d at 1950. The court seemed to base this conclusion on the high level of unpredictability in the field. In this regard, the court found (1) "in 1985, a person having ordinary skill in the art realized that the properties of bisphosphonates could not be anticipated based on their structure", (2) "each bisphosphonate has to be considered on its own" and (3) "[t]o infer from one compound the effects in another is dangerous and can be misleading." 90 USPQ2d 1951. Because there was no reasonable expectation of success, the court held that Teva had not established a prima facie case of obviousness.

Unexpected Results

The court further held that even if a prima facie case of obviousness had been established, certain results such as "the potency of risedronate" and the "low dose at

which risedronate was effective" were unexpected and therefore the claims were not obvious.

Practice Tip:

The Lead Compound Analysis continues to remain a valid argument when challenging a patent claim as being prima facie obvious either in litigation or by an Examiner at the USPTO. Rebuttal of this argument can be based on a number of factors including (1) the wrong "lead compound" was selected and (2) there is a high level of unpredictability in the field which supports an argument that there was no reasonable expectation of success. As a back-up, in case it is held that a prima facie case of obviousness has been established, evidence of the usual secondary considerations (especially unexpected results) should be presented.

CAN YOU REBUT AN OBVIOUSNESS ATTACK IF THERE ARE A LIMITED NUMBER OF UNPREDICTABLE SOLUTIONS?

Case: *Bayer Schering Pharma AG v. Barr Laboratories, Inc.*, 575 F.3d 1341, 91 U.S.P.Q.2d 1569 (Fed. Cir. 2009)

Discussion of the Case:

Bayer obtained U.S. Patent No. 6,787,531 ("the '531 patent") directed to an oral contraceptive composition comprising (a) micronized drospirenone particles; (b) α -ethinylestradiol; and (c) one or more pharmaceutically acceptable carriers, "the composition being in an oral dose form exposed to the gastric environment upon dissolution."

Prior to issuance of the '531 patent, drospirenone was known in the art for its contraceptive qualities. The issues associated with the use of drospirenone were also well-known. First, drospirenone is acid-sensitive and isomerizes when it is exposed to low-pH/highly acidic environments (i.e., human stomach). The resulting isomer does not exhibit anti-diuretic properties. Second, it is hydrophobic, which results in degraded bioavailability (e.g., the amount of active drug absorbed into the bloodstream and available to act on the body).

The usual solution for hydrophobic chemicals is to employ "micronization," wherein the drug's particle size is reduced, increasing its overall surface area and dissolution rate. However, "micronization" worsens acid sensitivities. Although it is known in the art to employ enteric-coated pills to overcome acid-sensitivity problems, this in turn leads to a further reduction in the drug's bioavailability.

During a study conducted in 1988, Bayer researchers noticed that, unexpectedly, a "normal" (e.g., unprotected) drospirenone pill and an enteric-coated pill exhibited the *same* bioavailability. Based on these findings, Bayer applied for and obtained the '531 patent.

Barr filed an Abbreviated New Drug Application (ANDA) with the FDA seeking approval to market a generic version of the drug. Bayer filed a patent infringement suit against Barr. Barr countered that the claims in the '531 patent were invalid as obvious.

Experts at trial confirmed that formulating the drug in the way described in the '531 patent (i.e., micronizing the drospirenone and omitting the enteric coating) should have increased isomerization, but instead had the opposite effect. However, despite expert testimony and evidence showing that the results were surprising and unexpected (which have customarily been sufficient to overcome a *prima facie* case of obviousness), the lower court ruled that Bayer's claims were invalid as obvious.

Using his "common sense", the District Court Judge concluded that the combination of elements was "obvious to try." Specifically, the lower court found that,

"[a]s in *KSR* "there are a finite number of identified predictable solutions" (e.g., (1) whether or not to employ micronization; and (2) whether or not to employ enteric coating)." Bayer appealed to CAFC.

On Appeal, and in a decision by Judge Mayer, CAFC applied the *KSR* standards and held that the formulations would have been obvious to a person having ordinary skill in the art due to the "limited" number of choices. Specifically, the Court noted that the skilled artisan only had two options to choose from: delivery of micronized drospirenone by a normal pill, or delivery of drospirenone by an enteric-coated pill.

In his dissent, Judge Newman sharply criticized the decision of CAFC, noting that "... [w]hat the law requires is not guesswork, not dumb luck, but a reasonable degree of predictability of success. My colleagues depart from the statutory standard, in ruling that persons of ordinary skill would have conducted experiments that were expected to fail...The exercise of judicial expertise to override the clear evidence of how persons of skill in this field actually behaved, is inappropriate."

Debatably, the ramifications of this case may present an example of the dreaded "slippery slope." *KSR* established that it is obvious to try something when there are a "finite" number of identified solutions. However, it could be argued that, in every single instance, there are only two options available: (1) the option of doing something, or (2) the option of not doing that same thing. Does *KSR* thus imply that every possible modification of an existent method or apparatus is obvious? Is *Bayer* opening the flood gates with regard to obviousness, or can it still be argued that the results of this case are limited to the facts therein?

Practice Tip:

When trying to overcome an "obvious to try"-type rejection, it is best to simultaneously attack all the grounds on which the rejection is based including that there are not (1) a limited number of (2) identified (3) predictable solutions. Relying only on the unpredictability aspect may not always be sufficient.

INTERPRETATION OF "PRODUCT-BY-PROCESS" CLAIMS

Case: *Abbott Labs. v. Sandoz Inc.*, 566 F.3d 1282, 90 U.S.P.Q.2d 1769 (Fed. Cir. 2009)

Discussion of the Case:

U. S. patent 4,935,507 (the '507 patent), of which Abbott is the exclusive licensee, claims a "crystalline [compound] which is obtainable by" either "acidifying a solution containing ...at room temperature or under warming" (claim 2) or "dissolving ... in an alcohol, continuing to stir the solution slowly under warming, then cooling...".(claim 5).

The term "crystalline" as used in the claims was interpreted as being limited to "Crystal A" for several reasons: (1) the Japanese priority application "strongly suggests that the '507 patent intentionally excluded Crystal B compounds", (2) the prosecution history of the '507 patent suggested that the claims were limited to Crystal A and (3) Crystal A was the only disclosed embodiment of the invention.

Regarding the interpretation of "product-by-process claims", the court, relying on old Supreme Court precedent, held that in order to infringe a product-by-process claim, the infringer must perform the recited process steps; affirming the prior case of *Atlantic Thermoplastics Co. v. Faytex Corp.*, 970 F.2d 834, 846-7, 23 USPQ2d 1481 (Fed. Cir. 1992) and overruling the prior case of *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 1583, 18 USPQ2d 1001 (Fed. Cir. 1991).

The court also held that the patentee could not avoid the narrow "product-by-process" interpretation by using "obtainable by" rather than "obtained by". In this regard the court stated "a patentee's use of the word "obtainable" rather than "obtained by" cannot give it a free pass to escape the ambit of the product-by-process claiming doctrine."

Finally, the court held that the claims did not literally read upon Lupin's product; the bulk of which was Crystal B, not Crystal A. The literal scope of the claims could not be expanded under the Doctrine of Equivalents to cover Lupin's product because of the prosecution history of the patent and also because of the "dedication doctrine that forecloses invocation of the doctrine of equivalents [because] applicant clearly knew of the Crystal B forms ... and disclosed them in its Japanese priority application ... [yet] declined to claim an embodiment expressly disclosed in its priority document." 90 U.S.P.Q.2d at 1781.

Practice Tip:

The PTO will likely continue to interpret product-by-process claims in the same "broad" manner as they have before, i.e., as covering any product that is the same as that obtained by the claimed process. However, it is now clear that "product-by-process" and "obtainable by" claims will be limited to the recited process steps. Thus, as before, patent

applicants should recite process steps in a product claim only as a last resort and only when there is no other way to distinguish the claims from the prior art.