

**Biotech and Pharmaceutical Patents at the
Federal Circuit: 2010 Year in Review**
Wednesday, January 19

John Garretson
Principal
New York office

J. Peter Fasse
Principal
Boston office

An Eventful Year...

FR

- Patentable subject matter
 - *Bilski v. Kappos*; *Prometheus v. Mayo*; *AMP v. Myriad*
- Written description and enablement
 - *Ariad v. Lilly*; *Alza v. Andrx*
- Inducement to infringe; kit claims; drug labeling
 - *AstraZeneca v. Apotex*

....*plus*

- Obviousness – *Sankyo v. Matrix Labs*; *Lilly v. Teva*
- Claim construction and DOE – *Intervet v. Merial*
- Best mode – *Ajinomoto v. ITC*

...*and looking forward to 2011* (*Therasense*, *Myriad*, *i4i*...)

Patentable Subject Matter

A teal square with the letters 'FR' in white, tilted slightly to the right.

Bilski v. Kappos, 561 U.S. __ (June 28, 2010)

- Not just a “business method” case
- § 101 provides broad patent eligibility but does not encompass laws of nature, physical phenomena or abstract ideas.
- The concept of hedging risk (and its application to energy markets) is an abstract idea, not a patentable process.
- The Federal Circuit’s “machine or transformation” test is not the exclusive test for assessing patentability.
- Implications for the medical field: e.g., biological parameters of disease states

Patentable Subject Matter

FR

Prometheus Laboratories, Inc. v. Mayo Collaborative Services (Fed. Cir., December 17, 2010) (“Prometheus II”)

- ***35 U.S.C. Section 101 - Inventions patentable***
 - Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.
- **A representative paraphrased claim:**
 - A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:
 - (a) administering a drug to a subject having the disorder; and
 - (b) determining the level of the drug in the subject,wherein the level of drug less than about X indicates a need to increase the amount of the drug subsequently administered to the subject and wherein the level of drug greater than about Y indicates a need to decrease the amount of the drug subsequently administered to the subject.

Patentable Subject Matter

A blue square logo with the letters 'FR' in white, tilted slightly to the right.

Prometheus II (continued):

- The District Court held that claims cover “correlations” between certain drug metabolite levels and therapeutic efficacy and toxicity and that these correlations were "natural phenomena," and thus unpatentable.
- The “administering” and “determining” steps are merely necessary data-gathering steps for any use of the correlations. However, an “unpatentable principle” will not be transformed into a “patentable process” simply by adding conventional method steps.
- In *Prometheus I* (2009), the Federal Circuit reversed and applied its recently-articulated *Bilski* rule stating that “[t]he proper inquiry under § 101 is whether these methods meet the Supreme Court’s machine or transformation test. The court held that they did.

Patentable Subject Matter

The logo consists of the letters 'FR' in a white, sans-serif font, centered within a teal-colored square that is slightly rotated clockwise.

Prometheus II (continued):

- Mayo requested that the Supreme Court review the decision after their recent *In re Bilski* decision. The Supreme Court vacated and remanded the Federal Circuit's Prometheus I decision.
- In Prometheus II (December 2010), the Federal Circuit again affirmed the District Court's conclusion that the Prometheus claims covered statutory subject matter under Section 101.
- The Federal Circuit held that the administering steps were transformative. "The transformation is of the human body following administration of a drug and the various chemical and physical changes of the drug's metabolites that enable their concentrations to be determined." These steps are essentially "method of treatment" steps, "which are *always transformative* when a defined group of drugs is administered to a body to alleviate the effects of an undesired condition" (emphasis added).

Patentable Subject Matter

A teal square with the letters 'FR' in white, tilted slightly to the right.

Prometheus II (continued):

- The Federal Circuit also found that the determining steps, by working a chemical and physical transformation on physical substances, likewise sufficiently confine the patent monopoly, as required by the machine-or-transformation test.

Patentable Subject Matter

The logo consists of the letters 'FR' in a white, sans-serif font, centered within a teal square that is slightly rotated clockwise.

Association for Molecular Pathology v. USPTO, Myriad Genetics and the Directors of the University of Utah Research Foundation
(U.S.D.C. S.D.N.Y., March 29, 2010) (“Myriad”)

- Plaintiffs - gene patents impede research
- Defendants - without patents, there is no incentive for private funding of the massive research required to get a genetic test approved and on the market
- Judge Sweet - said he could not resolve this sharp dispute of facts and policy (but he did....)

Patentable Subject Matter

The logo consists of the letters 'FR' in a white, sans-serif font, centered within a teal square that is slightly rotated clockwise.

Myriad (continued):

- **Two main types of claims at issue**

- Claims to isolated DNA (e.g., claim 1 covers an isolated DNA coding for a BRCA1 polypeptide having the amino acid sequence of SEQ ID NO:2. Claim 5 covers fragments of 15 nucleotides of the DNA molecule of claim 1 (BROADER than claim 1!).
 - Claims to methods of analyzing or comparing the BRCA1 gene to detect alterations.
- Judge Sweet agreed that DNA was a tangible chemical compound, but concluded that it was a "product of nature" and was not "markedly different" from the DNA found in nature, and was therefore not statutory subject matter under 35 U.S.C. 101 (relying on *Diamond v. Chakrabarty* (1980)).
 - According to Judge Sweet, DNA "serves as the physical embodiments of laws of nature - those that define the construction of the human body" even when isolated, and thus is an unpatentable product of nature. The purification of native DNA does not alter its essential characteristic - its nucleotide sequence - that is defined by nature.

Patentable Subject Matter

A blue square logo with the letters 'FR' in white, tilted slightly to the right.

Myriad (continued):

- The method claims fail the Federal Circuit "machine or transformation" test established in *Bilski*. Judge Sweet distinguished the claims in *Prometheus*, because the present method steps of "analyzing" and "comparing" are mental steps, as opposed to the *Prometheus* step of "determining" which required a physical sample to be taken.
- Judge Sweet rejected even screening claims as merely claiming a basic scientific principle that a slower rate of growth may indicate that the compound is a cancer therapeutic. The steps are merely data gathering, which does not make a mental process patentable.

Written Description

A teal square with the letters 'FR' in white, tilted slightly to the right.

Ariad Pharm., Inc. v. Eli Lilly & Co., 598 F.3d 1336 (2010)

- Trial court: JMOL of invalidity denied; CAFC reverses, then grants *en banc* review
- “Whether § 112, first paragraph, contains a written description requirement separate from the enablement requirement and, if so, the scope and purpose of the requirement”
- Held: § 112, first paragraph, contains a written description requirement separate from enablement (reversing trial court)

Written Description

The logo consists of the letters 'FR' in a white, sans-serif font, centered within a teal square that is slightly rotated clockwise.

Ariad v. Eli Lilly (continued):

- § 112, first paragraph contains two requirements: a written description (1) of the invention and (2) the manner and process of making and using the invention
- Applies equally to originally filed claims, where priority is not an issue

Written Description

FR

Ariad v. Eli Lilly (continued):

- **Broad principles:**
 - Does not demand examples or actual reduction to practice
 - Possession or reduction to practice outside specification not enough
 - Description that renders invention obvious does not satisfy requirement
 - Permits disclosure of structural features common to genus
 - Does *not* just apply to chemical and biological inventions
- **Ensures that when patent claims a genus by function or result, specification recites materials to accomplish the function/result**
- **Genus claims encompassing use of all substances that achieve result of reducing the binding of NF-kB to NF-kB recognition sites held invalid**
 - No examples of molecules capable of reducing NF-kB activity

Written Description

The logo consists of the letters 'FR' in a white, sans-serif font, centered within a teal square that is slightly rotated clockwise.

Ariad v. Eli Lilly (continued):

- Endorses existing PTO practice re written description
 - For biotech inventions, deposits can be used to help satisfy the requirement
 - For genus claims, have to describe a “representative number” of species
- But is there now an increased burden on applicants?
 - Examiners more likely to reject claims for lack of support
 - Examiners likely to require greater detail in the description
 - Examiners likely to require more disclosure of species to support genus claims
- The patent drafter must ensure that the written description covers the ***full breadth of the claims***
- Increased appeals and litigation are likely

Inducement to Infringe

The logo consists of the letters 'FR' in a white, sans-serif font, centered within a teal square that is slightly rotated clockwise.

AstraZeneca LP v. Apotex, Inc. (Fed. Cir., November 1, 2010)
 (“AstraZeneca”)

- Astra has two patents, both covering (1) methods of treating patients with respiratory diseases by administering a nebulized dose of budesonide (anti-inflammatory steroid) in a continuing regimen at a frequency of not more than once per day and (2) kits for treating respiratory diseases that include a certain amount of budesonide and a solvent, and a label indication administration by nebulization not more than once per day.
- The FDA approved Astra’s PULMICORT RESPULES® (budesonide suspension) in 2000 for once or twice daily administration. The label warns that patients should “titrate down” to the lowest effective dose.

Inducement to Infringe

The logo consists of the letters 'FR' in a white, sans-serif font, centered within a teal square that is slightly rotated clockwise.

AstraZeneca v. Apotex (continued):

- Apotex filed an Abbreviated New Drug Application (“ANDA”) seeking FDA approval for a generic version of budesonide for twice daily administration. Apotex asserted that it was not seeking approval for the once-daily method and that its proposed generic label would contain no explicit mention of once-daily administration.
- However, the proposed label retained the FDA-mandated downward-titration language found in Astra’s PULMICORT RESPULES® product label.
- The day after Apotex’s ANDA was approved, Astra filed a D.J. action and moved for a preliminary injunction. Astra argued that Apotex would directly infringe its kit claims and would induce infringement of its method claims by including the downward-titration statements in the proposed label.

Inducement to Infringe

The logo consists of the letters 'FR' in a white, sans-serif font, centered within a teal-colored square that is slightly rotated clockwise.

AstraZeneca v. Apotex (continued):

- Method Claims: “Whoever actively induces infringement of a patent shall be liable as an infringer.” 35 U.S.C. § 271(b). “[I]nducement requires that the alleged infringer knowingly induced infringement and possessed specific intent to encourage another’s infringement.” *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006) (*en banc* in relevant part).
- The court concluded that the proposed label would cause some users to infringe the method claims. For patients starting with the lowest dose, the downward-titration language would necessarily lead those patients to use the drug once-daily.
- Apotex had requested the FDA to allow it to add twice-daily dosing language or removing the downward titration language from its proposed label, but the FDA did not permit Apotex to make any of the suggested changes.

Inducement to Infringe

The logo consists of the letters 'FR' in a white, sans-serif font, centered within a teal square that is slightly rotated clockwise.

AstraZeneca v. Apotex (continued):

- Apotex alleged it faced an unfair “Hobson’s choice”: either comply with FDA requirements and risk a patent infringement suit or remove the downward-titration language and ensure that the ANDA would not be approved. The Federal Circuit saw no such dilemma. Apotex had three choices:
 - (1) wait until the patents expired before distributing the generic drug,
 - (2) appeal the FDA’s denial of Apotex’s proposed labeling amendments, or
 - (3) seek approval for a lower dosage strength of the drug.
- **Kit Claims:** The Federal Circuit agreed with Apotex that the claimed instructions here are not entitled to patentable weight. The instructions in no way function with the drug to create a new, unobvious product. Although FDA regulations require a label containing information needed for the safe and effective use of any drug, the Federal Circuit held that this is a requirement for FDA approval, not patentability.

Obviousness

A teal square with the letters 'FR' in white, tilted slightly to the right.

Daiichi Sankyo Company, Ltd. v. Matrix Laboratories, Ltd., Mylan Inc., et al. (Fed. Cir., September 9, 2010) (“Matrix”)

- Daiichi owns the '599 patent, which relates to angiotensin receptor blockers (ARBs) for the treatment of high blood pressure. Claim 13 of the '599 patent encompasses olmesartan medoxomil, a specific ARB marketed by Daiichi.
- Mylan filed ANDAs and challenged the patent. Daiichi responded with a suit for infringement. The parties stipulated to infringement of claim 13, leaving only Mylan’s counterclaim that claim 13 would have been obvious in light of second-generation ARBs in the prior art.

Obviousness

The logo consists of the letters 'FR' in a white, sans-serif font, centered within a teal-colored square that is slightly rotated clockwise.

Sankyo v. Matrix Labs (continued):

- Proof of obviousness based on structural similarity requires clear and convincing evidence that a medicinal chemist of ordinary skill would have been motivated to select and then to modify a prior art compound (e.g., a lead compound) to arrive at a claimed compound with a reasonable expectation that the new compound would have similar or improved properties compared with the old.
- In keeping with the flexible nature of the inquiry after *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), the motivation to select and modify a lead compound need not be explicit in the art.
- It is the possession of promising useful properties in a lead compound that motivates a chemist to make structurally similar compounds. Proving a reason to select a compound as a lead compound depends on more than just structural similarity, but also knowledge in the art of the functional properties and limitations of the prior art compounds.

Obviousness

A teal square with the letters 'FR' in white, tilted slightly to the right.

Sankyo v. Matrix Labs (continued):

- Altogether, the secondary prior art patent's SAR data and the structure of other second-generation ARBs counter any notion that one of skill in the art would have been motivated to modify the primary patent's compounds' lipophilic alkyl groups to a hydrophilic group. Such a holding would have been based on hindsight.
- The Federal Circuit affirmed the district court's findings that Mylan failed to establish both that
 - (1) one of skill in the art would have selected the ARBs of the primary reference as lead compounds, and
 - (2) one of skill in the art would have modified those supposed lead compounds at the 4-position of the imidazole ring to obtain olmesartan medoxomil.

Claim Construction and DOE

A teal square with the letters 'FR' in white, tilted slightly to the right.

Intervet, Inc. v. Merial Ltd. (Fed. Cir., Aug. 4, 2010) (“Merial”)

- Merial’s ‘601 patent relates to pathogenic “PVS-2” strains of porcine circovirus that cause postweaning multisystemic wasting syndrome.
- Patent specification discloses five separate PVS-2 strains:
 - All five were deposited with the ATCC
 - Complete nucleotide sequences of four strains listed in specification
 - Four listed sequences have 96% identity with prior art, non-pathogenic PVS-1 strains
- Specification also discloses 13 open reading frames (ORFs)
 - Nine ORFs are specific to PVS-2 strains
 - Four ORFs are shared by both PVS-1 and PVS-2 strains

Claim Construction and DOE

FR

Intervet, Inc. v. Merial Ltd. (continued):

- Representative claims:
 - 9. A vector comprising an isolated DNA molecule comprising a sequence selected from the group consisting of **ORFs 1 to 13** of **porcine circovirus type II**
 - 32. An isolated DNA molecule comprising a nucleotide sequence encoding an epitope which is specific to PCV-2 and not specific to PCV-1
- District Court claim construction:
 - **Porcine circovirus type II:** the five deposited nucleotide sequences
 - **ORFs 1 to 13:** the DNA sequences of the 13 ORFs in a particular SEQ ID listed in a table under Example 13 in of the patent
 - **Claim 32:** at least one DNA molecule unique to one of the five deposited sequences
- Summary judgment of non-infringement granted
 - Intervet vaccine DNA has 99.7% identity to deposited sequence, which is outside literal claim scope requiring strict identity to five deposited sequences

Claim Construction and DOE

The logo consists of the letters 'FR' in white, bold, sans-serif font, centered within a teal square that is slightly rotated clockwise.

Intervet, Inc. v. Merial Ltd. (continued):

- Federal Circuit reverses:
 - **Porcine circovirus type II:** the specification says the five deposited nucleotide sequences are *representative* of a **type** of porcine circovirus.
 - Invention not limited to just the five sequences -- a claimed genus can be broader than the representative disclosed species
 - No qualitative threshold for distinguishing PCV-1 and PCV-2 strains – depends on patterns of pathogenicity and sequence similarity
 - **Construction:** pathogenic pig virus 96% or more “homologous” to the four disclosed sequences, and about 76% or less “homologous” with the PCV-1 sequence
 - **ORFs 1 to 13**
 - Again, not just exact sequences disclosed in one table: (1) specification notes natural variation; and (2) district court’s construction would exclude two of the four sequenced PCV-2 strains
 - **Construction:** lengths of translatable DNA between pairs of start and stop codons, corresponding to the 13 ORFs identified in the patent specification

Claim Construction and DOE

FR

Intervet, Inc. v. Merial Ltd. (continued):

- Federal Circuit reverses:
 - **Claim 32.** An isolated DNA molecule comprising a nucleotide sequence encoding an epitope which is specific to PCV-2 and not specific to PCV-1.
 - **Not** limited to sequences physically derived from a non-PCV-2 source
 - “Specific to” means encodes at least one epitope found on PCV-2, but not PCV-1...doesn’t mean **only** found on PCV-2
 - **Claim 9.** A vector comprising an isolated DNA molecule comprising a sequence selected from the group consisting of ORFs 1-13 **of porcine circovirus type II.**
 - PCV-2: narrowing amendment related to patentability, but some Doctrine of Equivalents still permissible
 - No coverage for ORFs of pathogenic circoviruses found in other organisms, or of pathogenic strains of PCV-1
 - **But** Merial can still argue that a pathogenic porcine viral sequence with more than 99% nucleotide identity is equivalent to one of its five representative disclosed strains.

Claim Construction and DOE

A teal square with the letters 'FR' in white, tilted slightly to the right.

Intervet, Inc. v. Merial Ltd. (continued):

- Judge Dyk's partial dissent – implications for ***Myriad***?
 - Patentability of “isolated” DNA molecules...

Looking Forward to 2011...

The logo consists of the letters 'FR' in a white, sans-serif font, centered within a teal-colored square that is slightly rotated clockwise.

Therasense, Inc. v. Becton Dickinson & Co., No. 2008-1511,
(*en banc* review granted April 26, 2010)

- Trial court: found inequitable conduct (rendering patent unenforceable), based on failure to disclose statements made to European Patent Office that were deemed to contradict statements made to U.S. Patent Office
- Federal Circuit: affirmed (split panel decision)
- Panel majority said undisclosed contradictory statements made to EPO were: (1) material, and (2) made with intent to deceive.
- Judge Linn's dissent argued that Therasense offered plausible, detailed reasons why it believed the information withheld was not material, and that the nondisclosure was therefore not intentional.
- Federal Circuit subsequently granted *en banc* review.

Looking Forward to 2011...

The logo consists of the letters 'FR' in a white, sans-serif font, centered within a teal square that is slightly rotated clockwise.

Therasense v. BD (continued)

- **Six questions presented for *en banc* review:**
 - Should the materiality-intent balancing framework for inequitable conduct be modified or replaced?
 - If so, how? In particular, should the standard be tied directly to fraud or unclean hands? . . . If so, what is the appropriate standard for fraud or unclean hands?
 - What is the proper standard for materiality? What role should the U.S. Patent and Trademark Office's rules play in defining materiality? Should a finding of materiality require that but for the alleged misconduct, one or more claims would not have issued?
 - Under what circumstances is it proper to infer intent from materiality? . . .
 - Should the balancing inquiry (re materiality and intent) be abandoned?
 - Whether the standards for materiality and intent in other federal agency contexts or at common law shed light on the appropriate standards to be applied in the patent context

THE END

THANK YOU!