



Cohen Pontani Lieberman & Pavane LLP  
551 Fifth Avenue, New York, New York 10176  
(212) 687-2770, [www.cplplaw.com](http://www.cplplaw.com)

## UNDERSTANDING THE U.S. BIOTECHNOLOGY PATENT

Presented by Alan J. Morrison, Partner<sup>1</sup>  
Cohen Pontani Lieberman & Pavane LLP  
at  
Sun Yat-Sen University, Guangzhou  
June 16, 2009

### PATENTABLE SUBJECT MATTER

- Under 35 U.S.C. §101, patentable subject matter can be a “process, machine, manufacture, or composition of matter.”
- Products of nature, and natural processes, without some manipulation, are not patentable.
- Patentability must involve the “hand of man.”
- Example – Human anti-gp120 antibody is patentable subject matter if isolated, but *humanized* anti-gp120 antibody is patentable regardless of whether it is isolated.
- Example – Vitamin B<sub>12</sub> is not patentable subject matter, unless isolated (*Merck & Co. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156, 160 (4<sup>th</sup> Cir. 1958)).
- Example – Genetically modified bacterium is patentable subject matter (*Diamond v. Chakrabarty*, 447 U.S. 303 (1980)).

---

<sup>1</sup> This document solely reflects the views and considerations of the author, which should not be attributed to Cohen Pontani Lieberman & Pavane LLP or to any of its clients. © 2009.

- Example – An anti-sense molecule targeting a cancer-causing gene is patentable subject matter.
- Example – A method of treating Alzheimer’s disease is patentable subject matter, as are therapeutic and diagnostic methods generally.

*In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008)(en banc)

- *Bilski* involved a patent to a “method of managing the consumption risk costs of a commodity sold by a commodity provider at a fixed price” – i.e., a business method.
- The claims do not address a specific machine or apparatus.
- The resulting “*Bilski* Test” is as follows: A claim is patent-eligible if (i) it is tied to a particular machine or apparatus or (ii) it transforms a particular article into a different state or thing.
- *Bilski* is a Federal Circuit case. This case has been appealed to the U.S. Supreme Court that likely will hear the case later this year.
- There exist serious concerns as to how this case may affect biotech and pharmaceutical patents, especially those concerning diagnostic processes.

*Classen Immunotherapeutics, Inc. v. Biogen Idec*, 2008 U.S. App. LEXIS 25661 (Fed Cir. 2008) (non-precedential decision)

- *Classen* involved a patent to a method for evaluating vaccine immunization schedules by determining whether vaccination affects the incidence or severity of a disorder.
- No machine or transformation was involved.
- The Federal Circuit, applying *Bilski*, held – in an extremely brief opinion – that the method was not patentable subject matter under §101.

## UTILITY

- This issue is addressed almost entirely during prosecution rather than during litigation.
- §101 – a patentable invention must be useful.
- Use must be *substantial, specific and in currently available form*.

- Example – a method of making a new steroid compound having no disclosed use is not a useful method (*Brenner v. Manson*, 383 U.S. 519 (1966)).
- “[A] patent is not a hunting license.” *Id.*
- 2001 Utility Guidelines (64 Fed. Reg. 71,441) – a patentable invention must have a well-established utility. That is, (i) a person of ordinary skill would appreciate the invention’s usefulness, and (ii) the utility is specific, substantial and credible.
- Example – a genetically modified mouse useful only as snake food has no well-established utility, but one useful as a model for human cancer has well-established utility.
- Example – a DNA probe that hybridizes to a non-specified gene does not have specific utility, but a DNA probe that hybridizes to a human p53 gene does.
- Example – a DNA probe (e.g., EST) for conducting research to find target genes for treating disease does not have substantial utility, but a DNA probe that hybridizes to a human p53 gene does. Note: some EST’s can be patented if their uses constitute well-established utilities.
- Example – a method for “curing” AIDS would not have credible utility absent persuasive evidence to the contrary (i.e., successful human clinical trials), but a method for reducing the growth rate of a specified tumor would have credible utility assuming appropriate animal data are available.
- A patentable invention need only have *some* use.
- Utility is determined as of the filing date, but submitting *in vitro* and *in vivo* data during prosecution is a common means of overcoming utility rejections.
- Claiming a specific utility for a compound as a human therapeutic typically does not require actually demonstrating efficacy in humans.
- Example – A compound that is shown to affect blood pressure and relax smooth muscle cells in animals has utility, even though human therapeutic use was not demonstrated, since a correlation was established between test results and therapeutic activity. (*Nelson v. Bowler*, 626 F.2d 853 (C.C.P.A. 1980)).

## NOVELTY

- §102 – an invention lacks novelty if

- the invention was known or used by others in the U.S., or patented or described in a printed publication anywhere, before the invention by applicant (§102(a)); or
  - the invention was patented or described in a printed publication anywhere, or in public use or on sale in the U.S., more than one year prior to the application filing date [even if the disclosure is the inventor's own] (§102(b)); or ...
  - the invention was described in a U.S. patent or published in a U.S. patent application filed before the invention by applicant (§102(e)); or ...
  - the invention was first invented by another, in a NAFTA or WTO country, and not abandoned, suppressed or concealed (§102(g)).
- A prior art reference must teach all elements of a claim to anticipate it.
  - Loss of novelty can occur even if the disclosure is the inventor's own.
  - Example – Claim provides an isolated human monoclonal antibody that binds to gp120. Prior art reference teaches a human antibody preparation containing a mix of antibodies, one of which is a monoclonal antibody that binds to gp120. No anticipation.
  - A prior art reference must also be enabling to anticipate. (*Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 (Fed. Cir. 2003)).
  - Example – Claim provides an isolated human monoclonal antibody that binds to gp120. Prior art reference teaches an isolated human monoclonal antibody that binds to gp120, but in a prophetic manner such that before the filing date, one skilled in the art could not have actually isolated the antibody. No anticipation.
  - A prior art reference can anticipate by inherency.
  - Example – Claim provides the anti-histamine compound descarboethoxyloratadine (DCL). Prior art reference teaches loratadine. Loratadine is metabolized by the body to form DCL and thus, administration of loratadine to a subject (per its intended use) necessarily results in DCL. The claim is therefore anticipated. (*Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373 (Fed. Cir. 2003)).

*Impax Laboratories, Inc. v. Aventis Pharmaceuticals Inc.*, 545 F.3d 1312 (Fed. Cir. 2008)

- Impax filed an ANDA for riluzole tablets for treating amyotrophic lateral sclerosis (“ALS”).

- Impax sued Aventis for declaratory judgment that, *inter alia*, its '814 patent was invalid as anticipated.
- The '814 patent claims a “method for treating a mammal with [ALS], comprising the step of administering to said mammal in recognized need of said treatment an effective amount of [riluzole] or a pharmaceutically acceptable salt thereof.”
- Aventis' own '940 patent was one of the prior art references against the '814 patent. The '940 patent taught the use of a large genus of compounds (including riluzole) to treat many disorders, including ALS.
- Riluzole was “not meaningfully discussed” in the '940 patent. The '940 patent offers only “speculation” that compounds of this genus can treat ALS. The '940 patent also provides no evidence that riluzole would have been effective against ALS.
- The District Court found that the '940 patent did not enable treating ALS with riluzole.
- The Federal Circuit held that the claims are not invalid, noting that enablement is required for a reference to anticipate. This holding is consistent with earlier cases dealing with anticipation.
- A disclosed species anticipates a genus claim, but a disclosed genus *generally* does not anticipate a species claim.
- Example – Claim provides a specific oligonucleotide having a 5'-biotin label (i.e., the species). If the prior art reference teaches that same oligonucleotide, which can simply be “labeled” (i.e., the genus), there is no anticipation. If, however, the prior art reference teaches that the oligonucleotide can be 5'-labeled using any of 10 recited agents, one of which is identified as biotin, there is anticipation.
- Note: Claim sets should include narrow claims for important embodiments to ensure that at least some meaningful coverage remains if broad claims are invalid due to anticipation [or obviousness, etc. as discussed below].
- Example – claim 1 provides CCGTAACCGTA having a label, and claim 2 provides CCGTAACCGTA having a 5'-biotin label. If the prior art reference teaches “labeled CCGTAACCGTA”, claim 1 is anticipated but claim 2 is not.

## NONOBTAINABILITY OF BIOTECH INVENTIONS

- 35 U.S.C. §103 – an invention is not patentable if the differences between it and the prior art are such that the invention as a whole would have been obvious at the time of invention to a person of ordinary skill.
- Factors to consider include (i) scope and content of prior art, (ii) differences between the prior art and the invention, (iii) the level of skill in the art, and (iv) objective indicia of obviousness (i.e., secondary considerations such as unexpected results). (*Graham v. John Deere*, 383 U.S. 1 (1966)).
- A finding of “unexpected results” is “tantamount to a finding of nonobviousness.” *Hoganas AB v. Dresser Indus.*, 9 F.3d 948, 954 n.28 (Fed. Cir. 1993).
- Example – A method of making a predetermined protein using a heterologous DNA in a bacteria was held obvious in view of prior art teaching (i) use of rRNA gene as the heterologous gene and (ii) likely success of substituting the rRNA gene with a protein-encoding nucleic acid to make the protein. (*In re O’Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988)).
- Example – A hybridoma producing anti-human fibroblast interferon MoAbs was held obvious over prior art teaching successful methods of generating MoAbs to various other antigens. (*Ex parte Erlich*, 22 U.S.P.Q.2d 1463 (BNA) (B.P.A.I. 1992)).
- Example – Method of treating physical and emotional symptoms of PMS using fluoxetine was held non-obvious, since the prior art taught widespread failure of others to safely and effectively treat PMS. (*Eli Lilly & Co. v. Teva Pharmaceuticals USA, Inc.*, 2004 US Dist. LEXIS 14724 (S.D. Ind. July 29, 2004) *aff’d*, 2005 U.S. App. LEXIS 14583 (Fed. Cir. July 13, 2005)).

*KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007)

- In *KSR*, the Supreme Court held that a particular patent claim to a vehicle control apparatus was obvious.
- To be nonobvious, an invention must constitute an improvement over the art which is “more than the predictable use of prior art elements according to established functions.” *Id.* at 1740
- The Court held it to be error to rigidly rely on the “teaching, suggestion, or motivation” test (the “TSM” test). Under this test, a patent claim is only proved obvious if the prior art, the problem’s nature, or the knowledge of a person having ordinary skill in the art reveals some motivation or suggestion to combine the prior art teachings.

- The court also said that where a skilled artisan merely pursues “known options” from a “finite number of identified, predictable solutions,” obviousness under §103 arises.
- Until this year, a claim to a *particular* nucleic acid molecule (e.g., isolated human DNA) encoding a particular protein (e.g., human IGF) was not obvious over the amino acid sequence for that protein and known methods for isolating nucleic acids based on their encoded proteins. *In re Bell*, 991 F.2d 781, 785 (Fed. Cir. 1993) [holding was based on the degeneracy of the genetic code].
- In a related case, *In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995), the Court of Appeals held that “knowledge of a protein does not give one a conception of a particular DNA encoding it.” Also, “obvious to try” was held to be an inappropriate test for obviousness. *Id.* (but see *In re Kubin* below)

*In re Kubin*, App. No. 2008-1184 (Fed. Cir. 2009)

- *Kubin* applies *KSR* to the question of obviousness of DNA claims.
- The invention relates to Natural Killer Cell Activation Inducing Ligand (“NAIL”). The inventors discovered that NAIL binds to CD48. This discovery has important consequences for NK cells, e.g., increased cytotoxicity and interferon production. The invention relates to developing treatments for tumors and viral infections.
- The claims are to 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. SEQ ID NO:2 corresponds to NAIL.
- The prior art teaches “p38” receptor (found to be identical to NAIL), and an anti-p38 monoclonal antibody. There is no prior art teaching of the p38 (NAIL) amino acid or nucleic acid sequence.
- The prior art also teaches a method for molecular cloning in general.
- The court found that (i) there was motivation to combine these teachings, and (ii) there was a reasonable expectation of success regarding cloning the NAIL gene, based on the prior art.
- Under *KSR*, the “obvious to try” standard may be an appropriate test of nonobviousness.
- The U.S. and European approaches to determining non-obviousness and inventive step, respectively, for DNA claims are now more in sync.

- Drafting tip – unexpected features should be clearly identified as such in the patent application, and contrary teachings (i.e., teachings “away” from) stressed in the background section. That is, make your non-obviousness argument in the application.

#### ENABLEMENT, WRITTEN DESCRIPTION AND BEST MODE

- Under 35 U.S.C. §112, first paragraph, the specification must “contain a written description of the invention” and must “enable any person skilled in the art ... to make and use same, and shall set forth the best mode contemplated by the inventor of carrying out [the] invention.”
- These requirements must be satisfied as of the filing date.
- Written description is not the same as enablement. There still exists controversy as to whether these should be considered as distinct requirements.
- To satisfy the written description requirement, applicant must show “possession” of invention – i.e., allow one to visualize or recognize the identity of the subject matter purportedly described.
- Description of every species is not necessarily required, nor is *ipsis verbis* recitation in the application.
- Factors considered include
  - existing knowledge in the field,
  - extent and content of the prior art,
  - maturity of the technology, and
  - predictability of the aspect at issue.
- Example – If a claim provides a recombinant microorganism containing human insulin-encoding human cDNA, yet the description discloses only the human insulin amino acid sequence and a method for obtaining the human cDNA, the written description requirement is not satisfied. (*Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997)).
- Example – if a claim provides a method for selectively inhibiting COX-2 enzyme by administering a “non-steroidal compound that selectively inhibits activity of the COX-2 enzyme”, and the description discloses no such compounds, the written description requirement is not satisfied. (*Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 926 (Fed. Cir. 2004)).
- Example – Disclosing rat insulin-encoding DNA in the specification does not support a claim to all cDNA encoding vertebrate insulin. (*Univ. of Cal. v. Lilly*).

- Example – disclosure of a fully characterized antigen supports claiming an antibody specific to that antigen. (*Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2004)).
- Red Flag Terms – Care should be taken when using certain claim terms absent sufficient description – e.g., “homologous”, “functional analog”, “sufficient activity” and “structural variant.” This caveat also applies to the §112, second paragraph clarity requirement.
- To satisfy the enablement requirement, applicant must show how to make and use the invention. No undue experimentation can be required in order to practice the invention. But, routine experimentation is permitted. Courts may consider a number of factors to determine whether undue experimentation is required. (*In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988)).
- The specification must disclose more than a starting point for further research that might lead to the invention.
- *Wands* factors include
  - Quantity of required experimentation
  - Amount of guidance provided by the specification
  - Presence of working examples in the specification
  - Nature of the invention
  - State of the prior art
  - Relative skill of a person of “ordinary” skill in the art
  - Predictability or unpredictability of the art
  - Breadth of the claim
- Biological deposits can be used to satisfy the enablement requirement.
- The §101 utility and §112 enablement requirements are related, since one cannot teach how to use an invention if it has no use. Thus, utility and enablement rejections are typically issued jointly.

*Ariad Pharms., Inc. v. Eli Lilly & Co.*, 2009 U.S. App. LEXIS 6915 (Fed. Cir. 2009)

- *Ariad* involves gene regulation technology, namely NF- $\kappa$ B, a transcription factor that plays a role in expression of kappa immunoglobulin gene in B cells.
- The inventors discovered NF- $\kappa$ B’s role in controlling expression of various genes in response to stimuli. They also discovered that reducing NF- $\kappa$ B activity in cells can treat certain disorders.

- Ariad was the licensee of the '516 patent, claiming methods for reducing or altering NF- $\kappa$ B activity in cells, without stating how to do so.
- Ariad sued Lilly for infringement based on Lilly's Evista (osteoporosis) and Xigris (sepsis), alleging that they in fact reduced NF- $\kappa$ B activity.
- The '516 patent disclosed three classes of molecules: (i) "specific inhibitors" (of which none were identified); (ii) "dominantly interfering molecules" (of which none were identified); and (iii) "decoy molecules" (of which only hypothetical versions were identified, without specifying methods of use).
- The claims were held invalid for lack of written description.
- It is irrelevant that the claims are to a method rather than compounds per se. Claims to methods of reducing NF- $\kappa$ B activity must still satisfy the written description requirement as to what agents must be used, and how.
- A "vague functional description" and a "wish" for "future research" does not constitute written description of an invention.
- This holding is consistent with those of other written description cases in the biotech field, such as *Regents of the Univ. of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997) (a single rat insulin-encoding plasmid does not describe the genus of plasmids encoding all vertebrate insulins), and *Carnegie Mellon Univ. v. Hoffman-La Roche, Inc.*, 541 F.3d 1115 (Fed. Cir. 2008) (one DNA polymerase gene from one bacterial source does not describe all such genes from all bacterial sources).
- To satisfy the best mode requirement, applicant must disclose in the application the best mode contemplated by the inventor of carrying out the invention as of the filing date.
- Post-filing changes in the best mode do not negate initial compliance.
- Failure to satisfy the best mode requirement is seldom the basis of an invalidity holding.

#### ETHICAL OBLIGATIONS

- The duty of candor is key in U.S. practice.

- Patent applicants, as well as all associated individuals (attorney and others substantively involved with the application's prosecution), are obligated to disclose information material to patentability. Rule 1.56.
- Information Disclosure Statements are the means for satisfying this obligation, which continues so long as the application is pending.
- Failure to disclose material information, or the submission of materially false information, can constitute inequitable conduct if coupled with intent to deceive the Patent Office.
- A finding of inequitable conduct by a court renders a patent unenforceable.
- Examples of inequitable conduct can include the following acts if combined with an intent to deceive –
  - Submitting fabricated data,
  - Using the past tense to describe prophetic experiments,
  - Improperly including or excluding someone as an inventor,
  - Failing to disclose a material reference cited abroad during prosecution,
  - Failing to disclose adverse data, and
  - Improperly claiming small entity status (in pending and new applications) after a change to large entity status.

## INVENTORSHIP

- Inventorship requires conception and reduction to practice (actual or constructive).
- Conception can be sole or joint. §116.
- “Conception is the touchstone of inventorship, the completion of the mental part of the invention.” (*Burroughs Welcome Co. v. Barr Labs.*, 40 F.3d 1223, 1227-28 (Fed. Cir. 1994)).
- Conception requires a definite and permanent idea of the complete and operative invention.
- Example – An inventor need not know that an invention will work for conception to be complete. In *Burroughs*, the claimed invention was a method of treating AIDS in humans using AZT, based on animal but not human data. NIH scientists who subsequently tested AZT in humans and demonstrated efficacy were not co-inventors.
- Example – Providing a goal to be achieved without direction is not conception. A laboratory head instructing a post-doc to “find a way to increase CD4+ cell levels in HIV-infected subjects”, without providing guidance, has not conceived of a later-

claimed method of increasing CD4+ cell levels in HIV-infected subjects by administering compound X.

- Example – Carrying out confirming experiments does not constitute conception. For example, a laboratory assistant who tested prostaglandins on an animal model for glaucoma was not a co-inventor of a method for treating glaucoma in humans using prostaglandins, since (i) the animal model experiments were already determined by the named inventor to be desirable, (ii) the assistant’s efforts constituted routine work, and (iii) the assistant did not understand the effect of prostaglandins on glaucoma. (*Stern v. Trs. of Columbia Univ.*, 434 F.3d 1375 (Fed. Cir. 2006)).
- Incorrect naming of inventorship renders a patent invalid.
- Errors in naming inventorship can be corrected in a patent if made without deceptive intent. If deceptive intent is found, inventorship cannot be corrected and/or the patent can be held unenforceable.

#### CLAIM CONSTRUCTION

- Claim construction is a matter of law. (*Markman v. Westview Instr., Inc.*, 517 U.S. 370 (1996)). “*Markman* hearings” are now common for construing claims.
- Claim construction is also a predicate for invalidity and infringement determination.
- Procedure for construing claims is flexible and differs from court to court as to timing and approach.
- Generally, “intrinsic” evidence (i.e., patent claims, in light of the specification and file history) is given primary consideration, followed if necessary by “extrinsic” evidence (e.g., dictionaries and expert testimony). (*Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005)).
- A claim’s preamble may limit the claim, depending on the facts.
- Transition phrases have special meaning –
  - “consisting” – having what is recited and no more.
  - “consisting essentially of” – having what is recited and nothing more which materially affects the novel properties of the invention.
  - “comprising” – having what is recited and optionally more.

- Drafting Tip – Claims should include language accounting for all relevant forms of a therapeutic or routes of administration, etc. For example, a compound claim should include the molecule per se, its salts, and its pharmaceutical compositions. Treatment claims should include all appropriate routes of administration (systemic, iv, oral, topical, etc.), as well as biological effects (e.g., method of increasing CD4+ cells in a subject by administering agent X).

## PATENT INFRINGEMENT

- Direct infringement – making, using, offering for sale or selling a patented invention in the U.S., or importing a patented invention into the U.S. (§271(a)).
- Example 29 – A patent claims antibody X, and a third-party company sells antibody X in the U.S.
- Inducing infringement – inducing another to make, use, offer for sale or sell a patented invention in the U.S., or import a patented invention into the U.S. (§271(b)).
- Example 30 – a patent claims a method of treating a subject for cancer using antibody X, and a third-party company sells antibody X in the U.S. with a label for treating cancer.
- Contributory infringement – importing, offering to sell, or selling in the U.S. (i) a component of a patented article or composition, or (ii) a material or apparatus for practicing a patented process, constituting a material part of the invention, knowing same to be made or adapted for infringing such patent, and not suitable for any non-infringing use. (§271(c)).
- Infringement by supplying, or causing to be supplied, in or from the U.S. (a) all or a substantial portion of components of a patented invention so as to induce assembly abroad (§271(f)(1)), or (b) any component of a patented invention with the intention that the component will be combined abroad in a manner which would constitute contributory infringement if in the U.S. (§271(f)(2)).
- Infringement of a process patent by importing into the U.S., or offering to sell, selling or using a product made by the process. (§271(g)).
- Infringement can be literal or under the doctrine of equivalents. The doctrine of equivalents is tempered by a patent's prosecution history.

- Example –
  - Claim provides a peptide comprising the sequence Ala-Gly-Ser-Ser-Phe-Tyr, having apoptosis-inducing activity, and having a size of 1.5kD.
  - Accused product is a peptide comprising the sequence Ala-Gly-Ser-Ser-Phe-Tyr, having apoptosis-inducing activity, and having a size of 1.48kD.
  - Absent prosecution history to the contrary, the peptide likely infringes under the doctrine of equivalents even though it does not literally infringe.
  
- Example –
  - Claim provides a peptide comprising the sequence Ala-Gly-Ser-Ser-Phe-Tyr, having apoptosis-inducing activity, and having a size of 1.5kD.
  - Accused product is a peptide comprising the sequence Ala-Gly-Ser-Ser-Phe-Tyr, having apoptosis-inducing activity, and having a size of 1.48kD.
  - But, in the prosecution history, the originally filed claim was narrowed from “about 1.5kD” to “1.5kD” to overcome art teaching a 1.48kD peptide.
  - The peptide would not infringe literally or under the doctrine of equivalents.
  
- Example –
  - Claim provides a DNA molecule having the sequence GTAAGTGGCTAAGCTTAGC.
  - Accused product is a DNA molecule having the sequence GTAAGTATGGCTAAGCTTAGC (i.e., at least 90% homologous).
  - But, in the prosecution history, the originally filed claim was narrowed from “a DNA molecule having the sequence GTAAGTGGCTAAGCTTAGC, or a DNA molecule having at least 90% homology thereto” to the present claim of “a DNA molecule having the sequence GTAAGTGGCTAAGCTTAGC.”
  - The accused DNA would not infringe literally or under the doctrine of equivalents.
  
- Most common defenses to an infringement charge include noninfringement, invalidity and unenforceability.

## PATENT TERM

- For a U.S. patent issuing from an application filed on or after June 8, 1995, the term of the patent begins on the date of issuance and expires 20 years from the earliest claimed priority date, subject to any terminal disclaimers.
- For a U.S. patent issuing from an application filed before June 8, 1995, the term of the patent begins on the date of issuance and expires on the later of 17 years thereafter or 20 years from the earliest claimed priority date, subject to any terminal disclaimers.
- The term of a patent can be extended by up to five years due to delay caused by regulatory approval by the FDA (§156).

- The term of a patent can also be extended (“adjusted”) due to specified types of delay by the Patent Office in processing and examining the patent application. (Rule 1.701, et seq.).
- For biopharmaceutical patents, the final portion of patent term is often the most valuable, making patent term extension an important consideration.

#### CONTINUING APPLICATION PRACTICE

- U.S. practice permits the filing of one or more continuing applications that claim priority to a pending application.
- A continuing application must be filed while its parent application is pending, and must have at least one inventor in common with its parent application.
- There are three types of continuing applications: divisionals, continuations and continuations-in-part (CIP’s).
- A divisional application is filed to pursue claims that were not elected in response to a restriction requirement. That is, a divisional application claims an invention that the Patent Office has deemed independent and distinct from the invention elected for prosecution in the parent application. It shares the same specification and priority date with its parent application.
- A continuation application is filed to pursue subject matter disclosed in the parent application, but not yet claimed. It shares the same specification and priority date with its parent application.
- A CIP is filed to pursue claims to subject matter that may or may not have been disclosed in the parent application. Its specification contains new matter (e.g., experimental data and definitions) with respect to its parent application. A CIP has a “split” priority date – i.e., a priority date that is the same as that of its parent application regarding common subject matter, and a priority date as of the CIP filing date regarding the added subject matter.
- Biotech patent practice frequently employs filing continuing applications due to the multiple aspects of a given invention, thus giving rise to large patent families.
- Example –
  - A parent application as filed claims (i) an antibody useful as a diagnostic tool for cancer, (ii) a kit, (iii) a method of diagnosing cancer using the kit, and (iv) a method of making the antibody.

- Following a restriction requirement, invention (i) (the antibody) is elected, and the remaining claims are withdrawn.
  - Before issuance of the antibody patent, three divisionals are filed claiming the kit, the diagnostic method and the method of antibody production.
  - Before the diagnostic method patent issues, a continuation is filed to claim a method of diagnosing pancreatic cancer, which was disclosed but never claimed in the grandparent application.
  - At the end of prosecution, five patents have issued, all having the same specification and priority date.
- Caveat – Care should be taken when deciding to file a CIP to claim new subject matter, rather than filing a new application that is not a continuation. Filing a CIP in a situation where a new application could have been filed instead will result in needless loss of patent term.

#### PROVISIONAL APPLICATION PRACTICE

- U.S. practice permits the filing of a “provisional” patent application (§111(b)).
- A provisional application
  - need not contain any claims,
  - is not examined,
  - cannot claim priority of another application, although it can serve as a priority application for later filed regular applications,
  - becomes abandoned after 12 months from filing, and
  - is not counted when calculating patent term.
- Typically, a provisional application filing is followed after 12 months by a U.S. non-provisional or a PCT International Application designating the U.S.
- Since provisional applications effectively extend U.S. patent term by one year, these applications are almost always filed for inventions such as biopharmaceuticals where the expected product life exceeds 20 years, and the value of the patent at the end of its term is high.
- Caveat – Whenever possible, provisional applications should be filed as complete applications including claims, definitions and full discussion of the invention, rather than “skeletal” outlines. This helps ensure that the provisional application can serve as a priority document with regard to all aspects of the invention that might later be claimed.

## SAFE HARBOR UNDER 35 U.S.C. §271(e)(1)

- The Hatch-Waxman Act (“HWA”) was enacted in 1984 to eliminate two unintended distortions of effective patent term resulting from pre-market FDA approval.
- First, prior to the HWA, FDA review, which delays market entry, shortened the effective term of the FDA applicant’s patent.
- Second, prior to the HWA, a competitor’s activities regarding a patented invention constituted infringement, even if undertaken solely for the purpose of obtaining FDA approval. Thus, effective patent term was extended, at least de facto.
- The HWA addressed these distortions via 35 U.S.C. §§ 156 and 271(e)(1).
- §156 provides patent term extension for patents claiming a “product” subject to regulatory delays caused by FDA pre-market approval process. “Product” is a “drug product” and “[a]ny medical device, food additive, or color additive subject to regulation under the [FDCA].” §156(f).
- §271(e)(1) creates a “safe harbor” by exempting from infringement any making, using, offering to sell or selling in the United States or importing into the United States a “patented invention ... solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.”
- The Supreme Court has addressed the meaning of “patented invention” in §271(e)(1), holding, for example, that §271(e)(1) applies to medical devices and not just to drugs and additives. *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 669 (1990).
- The Supreme Court noted that §§ 156 and 271(e)(1) were “meant generally to be complementary.” *Id* at 673. That is, inventions covered by §156 are also to be covered under §271(e)(1), and those not covered by §156 are not to be covered under §271(e)(1). This statutory symmetry is preferable but not required. *Abtox, Inc. v. Exiltron Corp.*, 122 F.3d 1019 (Fed. Cir. 1997).
- The Supreme Court has also addressed the meaning of §271(e)(1)’s “reasonably related” in, e.g., *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005), holding that §271(e)(1) immunized the use of patented compounds in pre-clinical research even though the experimental results were never submitted to the FDA. (*Id* at 198-199).

*Proveris Scientific Corp. v. Innovasystems, Inc.*, 536 F.3d 1256 (Fed. Cir. 2008)

- Proveris holds the '400 patent, claiming a system and apparatus for characterizing aerosol sprays used in drug delivery devices. The device is useful in the FDA approval process, even though the device itself is not subject to FDA approval.
- Innovasystems ("Innova") makes the Optical Spray Analyzer ("OSA") device that is encompassed by the '400 patent. It is used for the FDA approval process, but is not itself subject to FDA approval.
- The Federal Circuit noted that Innova is not seeking FDA approval for its product in order to enter the market and compete with Proveris. Thus, the court held that §271(e)(1) (like §156) does not apply here, since Innova is outside the category of inventions for which §271(e)(1) was intended to provide relief.

#### ETHICAL ISSUES REGARDING HUMAN EMBRYONIC STEM CELL PATENTS

- This discussion highlights some of the ethical issues – as voiced by various segments of society – concerning hESC patents. These issues overlap with, but are distinct from, ethical issues concerning hESC research and commercialization.
- Why focus on ethical questions regarding hESC patents? hESC technology raises ethical issues beyond those for molecular inventions (e.g. DNA molecules) or non-embryonic stem cells. hESC's are at the center of the stem cell controversy, and are often equated with stem cells generally. This topic is a source of scientific and legal confusion.
- Ethical issues raised for hESC patents overlap with, but are distinct from, those for hESC – namely (i) funding (whether government money should be used to support hESC research), (ii) research (whether such work should be permitted, and if so, under what conditions), and (iii) commercialization (whether companies should be permitted to profit from hESC technology).
- A "patent" is a negative right to stop another from making, using, selling, offering to sell, or importing the claimed invention. A "hESC patent" is a patent claiming hESC's per se, or methods for isolating, using, or manipulating same. The patent concept is often misunderstood. It does not grant an "affirmative" right to practice claimed invention. Nor does it grant "ownership" of cells or body parts per se, whether inside or outside the body.
- A human embryo is generally considered to have "special" or "ethical" status. It has an individual's unique and total genome, and the potential to develop into a fetus.

- Should the status of a human stem cell depend on whether it was obtained from an embryo before formation of the primitive streak (e.g., per CIRM rules)? An embryo after formation of the primitive streak? A fetus? A fully grown person?
- To what extent should it matter whether a hESC comes from an intact embryo created solely for harvesting hESC's? An embryo discarded after IVF? An embryo destroyed in the process of isolating the hESC? Somatic cell nuclear transfer? A cell line previously derived from (i.e., many cell generations removed from) an intact embryo? A non-embryonic cell (e.g., an adult differentiated cell)?
- Should iPS cells be accorded special ethical status? If a stem cell originates from a non-embryonic cell, do ethical concerns arise if such stem cell is only "virtually" identical – but not identical – to cells isolated from an embryo? Do modifications to a hESC, whether genetic or otherwise, lessen its ethical status?
- Again, a patent is a negative right. A patent itself does not "destroy" embryos, or even grant an affirmative right to do so. Can a patent create a financial "incentive" to create and/or destroy more embryos? Or, is a patent merely a de facto requirement for commercializing hESC's? Is patenting problematic because it plays a role in "commercializing" or "objectifying" an embryo? Can it ever make sense to bar patenting a hESC while permitting hESC research (as is done in some European countries)?
- If hESC patents are ethically problematic, are these problems outweighed by existing or potential therapeutic uses? If so, which ones? Must these uses be life-saving (e.g., cancer or heart treatment), or can they simply be life-enhancing (e.g., cosmetic treatments)?
- In the U.S., hESC's and methods are patentable as compositions of matter and processes, respectively. Many patents have issued to date covering hESC's or related methods.
- No statute or rule limits the patenting of stem cells, embryonic or otherwise (as distinct from laws limiting research or funding). Case law exists that bars patenting inventions serving only immoral or illegal purposes, but has not been applied to hESC inventions. The WARF (Wisconsin Alumni Research Foundation) patent controversy is fact-specific and does not relate to the ethics of patenting hESC's. Rather, the WARF controversy involves questions of whether the patents are too broad and thus hinder scientific research, and whether the claims are patentable over the prior art.
- In Europe, approaches to hESC research differ, depending on the country. But, written patent prohibitions exist. Rule 28 EPC 2000 prohibits patenting an invention concerning "uses of human embryos for industrial or commercial purposes." Rule 28 conforms to Article 6 of Directive 98/44/EC. The WARF hESC application was rejected

in the EPO, since it was held to violate European patent law as of the filing date. However, a very different outcome may be possible for subsequent applications claiming inventions that, as of the filing date, do not require the destruction of an embryo.

- In sum, patent-related ethical issues overlap with, but are distinct from, ethical issues concerning hESC funding, research and commercialization. In the U.S. and abroad, many ethical questions regarding hESC technology remain, and are expected to change along with new technological developments.

#### PATENT REFORM LEGISLATION

- House Bill H.R. 1260 and companion Senate Bill S. 515 were introduced in March, 2009 and are pending. This proposed legislation stands to change the patent law in many ways – some good and others not.
- Some key provisions are
  - A first to file system replacing the first to invent system (this harmonizes the U.S. with other countries). A one-year grace period only for an inventor's own work. Derivation proceedings will replace interferences.
  - Creation of "cancellation" proceedings (analogous to Europe's opposition proceedings), in addition to providing *ex parte* and *inter partes* reexamination proceedings. Cancellation proceedings are to be conducted within 12 months of patent grant, before an administrative law judge (ALJ), based on any ground for invalidity except best mode. There would be no presumption of validity, and the challenging party would bear the burden of proof only by a preponderance of the evidence (rather than clear and convincing evidence). Cancellation proceedings would be concluded within one year, subject to extension of up to six months.
  - Creation of a new, proportionate damages calculation system (favoring accused infringers). This system is highly controversial, and is based on the invention's "specific contribution over the prior art."
  - Willful infringement cannot be pleaded until a court determines that the patent in suit is infringed, not invalid, and enforceable.
  - Granting the PTO additional fee-setting authority.
- Note – The pending legislation does not provide the PTO with additional, more substantive rule-making authority as did previous versions. However, this issue is

addressed in *Tafas v. Doll* below. Certain inequitable conduct provisions present in earlier versions are also absent from the pending legislation.

- The fate of the bills and their provisions is still uncertain.

#### PATENT RULES AND *TAFAS V. DOLL*

- In 2007, the PTO introduced a rules package on claim and continuation practice (also called the “Final Rule”).
- The package contained several rules that would fundamentally affect patent practice, especially relating to biotech and pharmaceutical inventions.
- Four of the proposed rule changes are as follows.
  - Rule 75 requires applicants submitting more than five independent claims or more than 25 claims in total to file an Examination Support Document (“ESD”). This is known as the “5/25” rule.
  - Rule 78 limits applicants to two continuation applications per application family absent a petition and a showing.
  - Rule 114 limits applicants to one Request for Continued Examination (“RCE”) per application family absent a petition and a showing.
  - Rule 256 establishes the requirements for an ESD.
- This package was widely criticized, especially by the biotech and pharmaceutical industries (e.g., for improperly limiting number of permitted claims and continuations), and would have severely harmed the biotech industry internationally.
- The rules package was temporarily enjoined from its November 1, 2007 implementation, and in 2008 was held void by a U.S. District Court.

#### *Tafas v. Doll*, App. No. 2008-1352 (Fed. Cir. 2009)

- On appeal, and in a split decision, the Federal Circuit, in *Tafas*, held that each of rules 75, 78, 114 and 256 is procedural and not substantive. That is, each rule alters the manner in which the parties present their viewpoints to the Patent and Trademark Office (“PTO”), but does not, on its face, foreclose effective opportunity to present patent applications for examination. So, according to the court, these rules are within the PTO’s rule-making authority.

- The Federal Circuit also held that Rule 78 (limiting the number of permitted continuations) is void as being contrary to 35 U.S.C. §120, the statute permitting the filing of continuing applications without limitation.
- The case was remanded to the District Court to determine, *inter alia*, whether any of the remaining rules (i) is arbitrary or capricious, (ii) conflicts with the patent statute in additional ways, (iii) is impermissibly vague, or (iv) is impermissibly retroactive.
- It remains unclear how the District Court will rule, what appeal will be sought, and whether the Patent Office will again attempt to pursue some or all of these rule changes in one form or another.