Patenting Nucleic Acid and Amino Acid Sequences in the United States

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Patentable Subject Matter

- An isolated and purified DNA molecule, RNA molecule, or amino acid molecule
  - isolated chemical compounds
- Full-Length Genetic Sequences
- Gene Fragments/ESTs
- SNPs
- Amino Acid Sequences

No Statutory Limit

- EPO
  - Article 53(a): inventions that are contrary to 'ordre public' or morality are not patentable
- US
  - Juicy Whip, Inc. v. Orange Bang, Inc., 292 F.3d 728 (Fed. Cir. 2002)
  - The USPTO is not in place to decide morals….

Four Statutory Requirements

- Patent Act of 1952
- An invention must be:

  - “USEFUL”

  - “NOVEL”

  - “NON-OBVIOUS”

  - “FULLY DISCLOSED/ENABLED”

Utility Requirements
35 U.S.C. § 101

- Diamond v. Chakrabarty, 447 U.S. 303 (1980)
  - genetically engineered bacteria are patentable
  - "anything under the sun that is made by man"
- The sequence must be isolated and purified from its natural environment
  - raw sequences with no known use are *not* patentable

Utility Guidelines

- Final revised guidelines issued January 5, 2001
  - www.uspto.gov
- Bar on utility substantially raised
  - Credible
  - Substantial
  - Specific

Credible Utility

- Would one skilled in the art believe that the asserted utility is true?
  - Cure for baldness/Prevention of Alzheimer's disease not credible absent definite data
  - Can prove utility with Declarative evidence
- Usually not questioned
  - Probes, chromosome markers acceptable
  - Lowest bar to utility; may not pass *specific* and *substantial* tests

Specific Utility

- Utility that is *specific* to the particular subject matter disclosed
  - contrast with *general* utility
- Gene Probe or Chromosome Marker
  - disclose a specific target
- Diagnostic tool
  - disclose a specific disease

Substantial Utility

- The “real world” use
- Basic research generally not patentable
  - A nucleic acid for studying the properties of the nucleic acid itself is not substantial
- “Throw away” utility
  - Amino acid sequence as a “nutritional supplement” or “shampoo ingredient”
  - Transgenic mice as “snake food”

Utility: Some Examples

- ESTs
  - Partial nucleic acid sequences can meet utility requirements if useful for diagnosis of a specific disease
- DNA fragment encoding a full ORF
  - Can meet utility requirements if homology to existing nucleic acids or proteins (with an *established* utility) is at least 95%

Written Description/Enablement
35 U.S.C. § 112, first paragraph

- The claimed invention must be:
  - described fully, clearly, concisely, and in exact terms
    - THE WRITTEN DESCRIPTION REQUIREMENT
  - so to enable one of skill in the art to make and use the invention
    - THE ENABLEMENT REQUIREMENT

Written Description

- The Regents of the University of California v. Eli Lilly and Company, 119 F.3d 1559 (Fed. Cir. 1997)
  - A description of a genus may be achieved by a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus

Written Description: Some Examples

- ESTs
  - partial cDNA sequence
  - SEQ ID NO:1 hybridizes to DNA indicative of disease
- Genes
  - regulatory elements, promoters, untranslated regions, introns
  - NOT described

Written Description: Some Examples

- Hybridizing Sequences
  - Highly stringent hybridization conditions
  - 6xSSC and 65^{o}C
  - Encode a protein having a specific function
- Allelic Variants
  - A genus of DNAs that encode Protein X (SEQ ID NO:2)
  - Generally difficult to obtain less than 95% sequence homology
  - Disclose as many variants as possible

Written Description: Some Examples

- Protein Variants
  - "amino acid substitutions, deletions, insertions, and/or additions"
  - extremely difficult to obtain without a good disclosure
- 95% sequence identity
- Retaining the protein function
  - disclose assay for identifying function

Enablement

- Undue Experimentation
  - unpredictability of the art
- Amgen, Inc. v. Chugai, 927 F.2d 1200 (Fed. Cir. 1991)
  - Amgen claimed all DNA sequences encoding human erythropoietin
  - Federal Circuit held that all variants were not enabled
  - Reliably predict the effect of the variations on the activity of the encoded protein

Constructing Claims to Sequences

- An isolated DNA sequence comprising SEQ ID NO:1.

- Comprising=Genus
  - any nucleic acid that minimally contains the SEQ ID NO, including the full-length gene, any fusion constructs or cDNAs
  - *must* disclose entire ORF
  - claim cannot read on a naturally occurring gene

Constructing Claims to Sequences

- An isolated and purified DNA sequence consisting of SEQ ID NO:1.

- Consisting of=Species
  - the actual nucleotides of the SEQ ID NO
  - partial sequences are not sufficient to claim a genus
  - lack of disclosure

Novelty

- Generally depends on the scope of the claims
- Draft of the human genome sequence (Celera Genomics)
  - *Science*, February 16, 2001
- Initial analysis of the human genome sequence (Human Genome Project)
  - *Nature*, February 15, 2001

Non-Obviousness
35 U.S.C. § 103

- Does the prior art suggest the claimed invention? Is there a reasonable expectation of success?

- In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995)
  - known amino acid sequence does not render a gene sequence *prima facie* obvious

Conclusion

- 35,000 to 45,000 genes ?
  - Smaller number of sequences up for grabs
  - Increase in Interference Proceedings
  - U.S. first to invent
- USPTO rules are evolving

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