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Examining Issues When Claiming Microarrays

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Examination Issues

- Utility (35 U.S.C. 101)
 - See Utility Examination Guidelines
 - 66 *Fed. Reg.* 1092 (Jan. 5, 2001)
- Written Description (35 U.S.C. 112, 1st para.)
 - See Written Description Examination Guidelines
 - 66 *Fed. Reg.* 1099 (Jan. 5, 2001)
- Enablement (35 U.S.C. 112, 1st para.)
- Novelty (35 U.S.C. 102)
- Nonobviousness (35 U.S.C. 103)



Utility

- **Brenner v. Manson, 383 U.S. 519 (1966)**
 - The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with **substantial utility**. Unless and until a process is refined and developed to this point -- where **specific** benefit exists in currently available form -- there is insufficient justification for permitting an applicant to engross what may prove to be a broad field



Utility

- **In re Fisher et al.** (CAFC, 14-1465, 09/07/2005)
 - Turning to the “specific” utility requirement, an **application must disclose a use which is not so vague as to be meaningless**. Indeed, one of our predecessor courts has observed “that the nebulous expressions ‘biological activity’ or ‘biological properties’ appearing in the specification convey no more explicit indication of the usefulness of the compounds and how to use them than did the equally obscure expression ‘useful for technical and pharmaceutical purposes’ unsuccessfully relied upon by the appellant in *In re Diedrich*.” *In re Kirk*, 376 F.2d 936, 941 (C.C.P.A. 1967). **Thus, in addition to providing a “substantial” utility, an asserted use must also show that that claimed invention can be used to provide a well-defined and particular benefit to the public.**



Utility Concerns for Nucleic acid microarrays.

- Conventional DNA microarrays are designed using oligonucleotide probes or complementary DNA (cDNA).
- Oligonucleotide can be synthesized *in situ* or via conventional DNA synthesis and later attached to the chip surface.



Utility... cont

- Hybridization of labeled sample DNA via complementary sequences allows the determination of the level of gene expression in the sample tested.
- If the nucleic acids on an array lack utility, it is likely that the nucleic acids simply by virtue of being arranged on the microarray will not have utility.



Utility- cont.

- Microarrays are often designed as research tools and may lack patentable utility.
 - Arrays based on ESTs
 - Arrays based on cDNAs
 - Gene profiling- the detection of differential gene regulation due to a treatment or disease condition
 - Detection of natural polymorphism, e.g., Single Nucleotide Polymorphisms or SNPs



Utility-cont.

- Mutation detection via Microarrays with proper controls may meet the utility requirements.
 - May indicate a predisposition to a specific genetic disease if data supports a correlation to the disease or phenotypic state.
- Take home message-
 - If the nucleotide sequences lack utility- the microarrays are often found to lack *prima facie* utility.



Utility- cont.

- Method of using microarrays may meet standards for compliance with the utility requirement of 35 U.S.C.101.
 - A method of predicting patient drug response
 - Personalized medicine on a chip
- Utility of these methods is dependent on proper demonstration of proper controls.



Written Description

- Can one skilled in the art reasonably conclude that the inventor was in possession of the claimed invention at the time the application was filed?
- Written description requirement is separate and distinct from the enablement requirement.



Written Description

- The specification shall contain a **written description** of the invention, and of the manner and process of **making and using** it, in such full, clear, concise, and exact terms as to enable any person...
- **Federal Register:**
 - (http://www.access.gpo.11gov/su_docs/aces/aces140.html)
 - Written Description Guidelines:
 - 66 FR 1099 (January 5, 2001)



Written Description-cont.

- Microarrays are composed of nucleic acids immobilized on a stable surface and are used to detect hybridization to complementary nucleic acids.
 - will have the same written description issues as nucleic acids.
- % homology/identity claims or hybridization language may raise issues under Written Description requirement of 35 U.S.C. 112, first paragraph.



Written Description- cont

- A common method of denoting the sequences on a microarray are by Genbank accession numbers
 - however, accession number are not fixed entities and can change over time.



Enablement

- Enablement
 - Specification must teach how to make and use the full scope of the claimed invention without undue experimentation.
 - Apply factors set forth in *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)
 - Breadth of the claims
 - Nature of the invention
 - State of the prior art
 - Relative skill of those in the art
 - Amount of direction provided by the inventor(s)
 - Level of predictability in the art
 - Existence of any working examples
 - Quantity of experimentation needed



Prior art Issues

- Term “microarray” is used in a generic sense.
 - collection of nucleic acids on a solid support
 - Southern blots, dot blots, colony lift can all be considered “microarrays” and prior art teaching the nucleic acids on the microarray are considered applicable.
- In the absence of unexpected results specifically claimed requirements of microarrays may be considered as obvious, including:
 - specific density requirement
 - specific oligo sequences



Other Issues

- Data Mining
 - Large amounts of data can be generated by these technologies.
 - There is a lack of standards for the collection and presentation of microarray data.
 - There are neither current standards for the exporting of data nor protocols for dealing with the differences between databases.



Restriction & Search

- Example
 - Specification discloses 11,000 genes
 - Claims to a microarray with at least 100 of the 11,000 genes
 - Possible gene combinations would be too innumerable to examine
 - Examiner would require applicants to elect a single gene sequence from the combination for examination purposes.



Restriction & Search

- Burden of Search-
 - a single combination of nucleotide sequences will generally not be subject to a restriction requirement but may be subject to a species election.
 - one novel and nonobvious sequence within the combination will render the entire combination free of the prior art.
- The identification of any allowable sequence(s)
 - will cause all combinations containing the allowed sequence(s) to be allowable over the prior art.



Microarray Composition Claims

- USP 6,500,938 Au-Yound et al.
 - 1. A combination comprising a plurality of polynucleotide probes, wherein said plurality of probes are SEQ ID NOs:1-1490.
 - 2. The combination of claim 1, wherein said plurality of probes are complementary DNAs.
 - 3. The combination of claim 1, wherein said plurality of probes are clone DNAs.
 - 4. The combination of claim 1, wherein said plurality of probes are immobilized on a substrate.
 - 5. The combination of claim 4, wherein said plurality of probes are hybridizable array elements in a microarray.



Microarray Method Claim

- USP 6,607,879 Cocks et al.
- 1. A composition comprising a plurality of cDNAs for use in detecting the altered expression of genes in an immunological response, wherein said plurality of cDNAs comprises SEQ ID NOs:1-1508 or the complete complements thereof.
- 2. The composition of claim 1, wherein said cDNAs are immobilized on a substrate.
- 3. The composition of claim 1, wherein said cDNAs are hybridizable elements on a microarray.
- 4. A method for diagnosing or monitoring the treatment of an immunopathological condition in a sample, said method comprising:



Microarray Method Claim

- a) obtaining nucleic acids from a sample;
- b) contacting the nucleic acids of the sample with an array comprising the plurality of cDNAs of claim 1 under conditions to form one or more hybridization complexes;
- c) detecting said hybridization complexes; and
- d) comparing the levels of the hybridization complexes detected in step (c) with the level of hybridization complexes detected in a non-diseased sample, wherein the altered level of hybridization complexes detected in step (c) compared with the level of hybridization complexes of a non-diseased sample correlates with the presence of an immunopathological condition.



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