-----Original Message-----
From: Wight, Chris
Sent: Wednesday, October 10, 2007 9:22 AM
To: Markush.Comments
Subject: Comments in Response to Proposed Rules Relating to Alternative Claim Language

Comments in Response to Proposed Rules Relating to Alternative Claim Language

The following comments are submitted in response to the USPTO proposed rules relating to examination of patent applications that include claims containing alternative language. The proposed rules were published on August 10, 2007, in the Federal Register, Vol. 72, No. 154, pp. 44992-45001.

These comments reflects the opinions and views of the submitter, and should not be attributed, in whole or in part, to Brinks Hofer Gilson & Lione, any of its attorneys, or any of its clients. In the event that any of these comments are published, the submitter requests that the comments be published anonymously.

Comments Regarding 37 CFR §1.140

Rule 1.140(a)(1) - "Share a substantial feature"

It is proposed that Section 1.140 be revised to require that a claim that reads on multiple species using alternative language be limited to a "single invention," which must meet at least one of the following two conditions:

(1) The species share a substantial feature essential for a common utility, or
(2) The species are *prima facie* obvious over each other.

It is submitted that the standard of "*substantial feature essential for a common utility*" is potentially indefinite and/or incomplete. In the Supplementary Information section of the proposed rules, Section B, it is stated that alternative claim language is generally used in two different contexts: (1) chemical compounds, and (2) process steps or components. With respect to the use of alternative claim language in chemical compound cases, it is noted that the current practice, as articulated in MPEP 803.02, provides that "unity of invention" was satisfied where

compounds “(1) share a *common utility*, and (2) share a *substantial structural feature* essential to that utility.” With respect to process steps or components, on the other hand, it is stated that current practice permits Markush format if all the members of the groups “possess at least one *property* in common which is mainly responsible for their *function* in the claimed *relationship*, and it is clear from their very nature or from the prior art that all of them possess this property.” (Citing MPEP 2173.05(h)) Thus, the unity of invention standard proposed for Section 1.140 (“*substantial feature* essential for a common utility”) could be construed as being limited to the standard articulated for compounds (“substantial *structural* feature”), and not to the standard articulated for process steps or components (“at least one *property* in common which is mainly responsible for their *function* in the claimed *relationship*”). Although standard dictionary definitions of the term “feature” encompass such terms “property,” “function,” and “relationship,” it is possible from the context of the proposed rule making that the language of proposed Section 1.140(a)(1) could be misinterpreted as being limited to common *structural* or *physical* features, and does not contemplate common *properties* or *relationships* that may be difficult or impossible to characterize as being structurally or physically related.

In order to avoid such an erroneous interpretation, it is recommended that the language of Section 1.140 be revised to reflect consideration of both structural features of compounds, as well as properties, characteristics and relationships of components of process steps. Alternatively, in the event that the language of proposed Section 1.140 is limited to the term “feature,” it is recommended that the final rules clarify that the term “feature” contemplates and encompasses “properties,” “characteristics,” and “relationships” of components utilized in process claims.

By way of example, the above clarification is important in inventions relating to discovery of genetic variations (including those commonly referred to as "single nucleotide polymorphisms" or "SNPs") that are associated with a particular disease. Many diseases are caused by genetic variations (SNPs) that are genetically inherited. Some diseases may be caused by a single SNP in an individual’s DNA, while other diseases may be caused by multiple SNPs. Diagnosis of the disease (or risk of developing the disease), however, is not limited to detection of only SNPs that *cause* a disease. Because large regions of DNA are often inherited as blocks which contain both causal and non-causal SNPs, non-causal SNPs are often co-inherited with causal mutations, and the presence of *non-causal* SNPs may also be predictive of a disease. Thus, in many genetic studies using blood samples from patients having a particular disease (together with control samples from patients who do not have the disease) particular SNPs are identified in the patient’s DNA that

are statistically correlated with the disease. In addition, for each SNP that is experimentally determined to be associated with the disease, there are numerous additional SNPs that are physically proximate to the experimentally identified SNP and are nearly always genetically inherited together as a block in a particular population of individuals. Such a region is referred to in the field of genetics as a "linkage disequilibrium block" or "LD block." Linkage disequilibrium means that, relative to the frequency of random combinations of alleles (“equilibrium”), a particular combination of SNPs at two or more different SNP sites occurs more frequently (“disequilibrium”). Therefore, when a SNP is in "linkage disequilibrium" with another SNP, the presence of the first SNP indicates a statistically significant probability that the other SNP will also be present. Because the frequency of co-inheritance is a function of physical recombination events, there is a higher probability that physically proximate SNPs will be co-inherited than SNPs that are physically distant. Thus, linkage disequilibrium is generally, but not exclusively, a measure of physical proximity of the two SNPs in a chromosome. Since SNPs that are in linkage disequilibrium are inherited together with a frequency that is statistically significant, the presence of one SNP provides similar predictive information as another SNP in the same LD block. SNPs within the same LD block may therefore be substituted for each other as markers or predictors of disease.

Though the various SNPs located within a single LD block share a common physical relationship (they are present on the same strand of DNA), each SNP has a unique physical location and so does not necessarily share a common molecular structure. All the SNPs within a single LD block, however, share a common property, characteristic or relationship, in that they are physically proximate to each other in a well-defined region of DNA, and all have a statistically significant correlation with a disease as a result of being co-inherited as a physical block. In this instance, the class of SNPs present in a single LD block should be grouped together as a single invention. The statistical correlation linking SNPs together in a physical region called an LD block constitutes a common property or relationship that, though related by physical proximity, is not strictly defined in terms of structural similarity, but rather a common association or correlation that is a function of their physical proximity.

How SNPs within a single LD block are treated for purposes of the “single invention” rule is critical. The ability to claim a group of SNPs that are located in a common LD block (which typically number in the hundreds or thousands) is essential to protecting the investment in genetics research. Because each SNP within an LD block is similarly predictive of the disease (though perhaps not equally predictive, since all SNPs in an LD block may not be in 100% disequilibrium), any one SNP within the

same LD block may be substituted for any other SNP in a genetic test. In order to obtain meaningful patent protection, each and every SNP within an LD block must be covered by some patent claim. If each individual SNP were considered to be a separated and distinct invention, the cost of prosecuting thousands of such applications would be economically prohibitive. Accordingly, as a practical matter, it is critical that a single invention be defined as multiple SNPs in a single LD block that are associated with a disease.

It is, therefore, recommended that the final rules clarify that a single invention may encompass alternative species that possess a common property or relationship, such as a collection of SNPs that are in linkage disequilibrium.

"One sequence per application" Rule

The proposed rules on alternative claim language should also clarify how the rules will be applied to the "one sequence per application rule," currently being applied by the USPTO in cases involving claims to nucleotide sequences. Specifically, will the "one sequence per application rule" be construed to permit a single method claim, as described above, to recite multiple SNPs that are in linkage disequilibrium?

As explained above, the discovery of an experimentally derived SNP and the identification of an LD block within which that SNP and hundreds or thousands of other SNPs is located, enables genetic testing for a disease using any one or more of the SNPs in the LD block. As research progresses, particular combinations or subcombinations of SNPs may be discovered that are more predictive of the disease (and which may constitute a separately patentable invention, based on a higher level of predictability). However, at present, the experimental identification of a single SNP generally enables identification of multiple additional SNPs in the same LD block as the experimentally identified SNP, all of which have a statistically significant correlation with the disease. Thus, although a group of SNPs in a single LD block defines a class of distinct physical features (SNPs located at different locations), the SNPs share a common utility (association with a disease) that is predicated on the SNPs having a sufficiently close physical proximity that they are related by genetic co-inheritance (linkage disequilibrium).

It is proposed that the rules or comments on the final rules clarify application of the "one sequence per application" rule, and specifically clarify that claims that recite methods of *using sequence information* are not necessarily subject to the "one sequence per application rule" (in contrast to composition of matter claims that relate to the *polynucleotide compositions* themselves). Methods of using a one or more of a plurality of

SNPs that are in linkage disequilibrium restricts the class of SNPs on the basis of their physical proximity, common utility, and shared relationship as co-inherited genetic markers that are predictive of the same disease.

Comments Regarding Proposed Amendments to 37 CFR §1.75

Rule 1.75(j) - "Number of alternatives in the claim"

The proposed rule making also proposes that 35 CFR 1.75(j) be amended to require that any claim reciting multiple species by using alternative language meet the following requirements:

(1) The number and presentation of alternatives in the claim does not make the claim difficult to construe;

(2) No alternative is defined as a set of further alternatives within the claims; and

(3) No alternative is encompassed by any other alternative within a list of alternatives, unless there is no other practical way to define the invention.

(4) Each alternative within a list of alternatives must be substitutable one for another.

The scenario described above, involving a claim reciting a method of determining a patient's risk of disease by detecting the presence or absence of one or more SNP located within a defined LD block, also raises a practical issue of whether a prior art search of each SNP recited in such claims would constitute a significant burden on the examiner. A process claim that recites a method of detecting the presence of *one or more* of hundreds or thousands of SNPs in the same LD block will, for example, likely require a prior art search of each and every SNP recited or known to exist in that region of DNA defined by the LD block. Although individual searches of each SNP would likely constitute a significant burden for examiners, sophisticated bioinformatics software is available that can perform such searching with little difficulty.

It is recommended that the rules address such issues as how applicants may assist examiners in conducting searches that ameliorate the search burden on the examiner.

Rule 1.75(k) - "Claim may not incorporate another part of the specification"

The proposed rule making further proposes that 37 CFR 1.75(k) be amended to require that "a claim may not incorporate another part of the specification or drawings by reference, unless there is no other practical way to define the invention."

As explained above, in claims that recite a method of determining a person's risk of disease by detecting the presence or absence of one or more SNP in a particular LD block, the LD block will often encompass hundreds or thousands of SNPs. Claims may utilize a functional definition of LD block (i.e., "one or more SNP that is in linkage disequilibrium with SNP X"), a structural definition of LD block (i.e., "one or more SNP that is in the LD block defined by nucleotides X-Y of chromosome Z") or a Markush group (i.e., "one or more SNP selected from the group consisting of the SNPs of Tables 1-10"). As a practical matter, patent applications will likely include claims of each of the above formats, since each format represents an alternative way of defining similar subject matter of the invention. Genetic studies used to experimentally identify SNPs associated with a disease now commonly utilize silicon chips that include hundreds of thousands or millions of SNPs derived from SNP databases. Due to the limited capacity of such chips, not all known SNPs are present on the chips. Consequently, the experimentally derived SNPs may not represent all SNPs that are associated with a disease. Claims that recite specific SNPs in a given LD block will also not likely represent all possible SNPs in the LD block, since the SNPs in given LD block represent only those that have been added to the SNP databases to-date; as genetic studies of additional individuals and other populations is conducted, additional SNPs are likely to be discovered. Accordingly, a list of SNPs in a given LD block is merely representative of possible SNPs within the LD block. A functional definition is, therefore, likely to be broader, encompassing SNPs in the same LD block that are subsequently discovered, or that are known but simply not yet included in the SNP database. Claims that recite specific SNPs by name in a table, however, remain valuable, since they define the subject matter more particularly, without relying on functional criteria.

Because claims that recite specific SNPs in a particular LD block cannot practically recite hundreds or thousands of SNPs within the claim itself, it is proposed that the new rule making specifically articulate standards that are more objective than "no other practical way to define the invention," or at least provide representative examples of claims that satisfy (or do not satisfy) this criteria.

Christopher L. Wight
Brinks Hofer Gilson & Lione
405 S. Main Street, Suite 800
Salt Lake City, UT 84111-3400
801.333.7905 Direct

801.355.7901 Fax
801.979.7219 Mobile
cwight@usebrinks.com
www.usebrinks.com