Comment 42 Nat'l Adv. Counc. Human Genome Res., NIH/Burke et al.

March 21, 2000

Box 8
Commissioner of Patents and Trademarks
Washington, DC 20231
Attention: Mark Nagumo mark.nagumo@uspto.gov

Dear Commissioner:

This letter is in response to the request for public comment concerning the Revised Utility Examination Guidelines published in the Federal Register, Vol 64, No 244 [Docket No. 991027289-9289-01]. The criteria covering the issuance of patents on genes and genomes, particularly on human genes and the human genome, is a matter of great concern to us as members of the National Advisory Council for Human Genome Research of the National Institutes of Health.

We recognize the considerable thought that has gone into the Revised Guidelines, and we applaud the steps you have taken toward requiring more specific utility in granting patents for DNA sequence. We agree that proposed uses of DNA sequences as genetic markers and probes to recover larger fragments are insubstantial. We also agree that patents should be granted when the function of gene is revealed specifically through the acquisition of new data, e.g. the gene responsible for cystic fibrosis.

We strongly disagree, however, with allowance of broad claims in patents on human genes that extend to utilities not demonstrated in the patent. In this situation, we believe a broad allowance of claims is unjustified and will strongly discourage the further research efforts that will be necessary to translate gene discovery into medically important therapies. To avoid stifling scientific discovery and commercial application, we believe that allowances in these instances must be restricted to those utilities that are enabled by the patent.

Finding partial sequence similarity is an obvious and non-inventive step. To show lack of obviousness requires direct evidence that distinguishes the putative new ligase from the other known family members. Extending similar reasoning to the establishment of "significant, substantial and credible utility," it could be argued *a priori* that every gene (excluding pseudogenes) can be assumed to have utility, until the opposite is shown, on the basis that each gene has been selected and preserved by evolution. The latter position would require a patent officer to show that a new gene does not have a function. We maintain that the inventive step necessary for broad claims is the discovery of the specific role the gene performs in biological processes, remembering that it is possible that a DNA sequence may be an evolutionary vestige and have no biological role in the organism. The molecular identification of a gene with a function already established genetically (e.g., a gene that controls eye color or that can lead to a particular disease) could constitute a patentable invention with broad claims, in our view,

because the biological role would already be known. On the other hand, a statement that a new gene probably encodes a ligase, even if this statement is later substantiated, should not be accepted to support broad claims, because the evidence does not reveal anything about the role, or roles, of the ligase in biology; there are several ligases known, and each plays particular and distinct biological roles. It is the knowledge of the specific biological role(s) of the new gene that adds value over and above predicting, and even confirming, the predicted ligase function. Knowledge that a gene has partial or even striking similarity to a ligase does not, in and of itself, enable any specific utility for that gene. Furthermore, many genes function at multiple times and sites; a patent specific for one function of a particular gene should not preclude patents based on the subsequent discovery of utility based upon functions unanticipated in the original application.

We consequently maintain that the granting of a patent based solely on an assigned partial sequence identity with known genes should be subject to strict limitations on allowed claims. If a probable function based on partial sequence identity is to be allowed, then we believe that the allowed claims should be restricted to the utilities that are actually or reasonably enabled by the discovery. Thus, in your Example 10, the identification of a new member of the ligase family, the only claims allowable should be those related to the use of the ligase in joining oligonucleotides or in screening for inhibitors of the ligase, claims that are reasonably enabled by the new discovery. Allowable claims should not cover speculative uses that are not enabled by the discovery, such as using inhibitors of the ligase to treat any disease in which the ligase may later be found to play a role. Such a limitation provides appropriate reward for the invention yet does not allow claims that go well beyond the invention that would discourage further research to identify other potential utilities. We believe that additional utilities, when discovered, should be the subject of subsequent patents. We believe this approach is consistent with the PTO's approach in other fields, which serves to promote, rather than discourage, innovation and commerce.

An example of speculative broad claims, which were in our opinion inappropriately allowed, is seen in the recently granted patent on CCR5. Based on sequence similarity, a patent was granted on a new gene that was claimed to be a putative chemokine receptor. No evidence was given to define the ligand or for any biological role for the putative receptor, but broad claims about the utility of the receptor were allowed. The allowed patent included a statement that CCR5 could be a receptor for a virus (a claim that could be made for any cell surface molecule). Independent of knowledge of the filing of the patent, other investigators established that CCR5 is the key co-receptor for HIV, making CCR5 a very important potential drug target. The patent taught nothing that contributed to these later important discoveries, but now the holders can dominate the field. Moreover, this broad allowance makes no concession to the discoverers of the key piece of intellectual property, namely that CCR5 is an HIV co-receptor. Allowing broad, poorly substantiated claims creates, *de facto,* an unacceptable monopoly on all fields in which the new gene might be found to be of use.

It is instructive to compare Example 10, requesting a patent on a new putative ligase, with a hypothetical request for a patent on a novel chemical inhibitor of a ligase. It would be expected generally that, in the latter patent, claims for treatment of diseases would be allowed even if no proof was offered that the ligase played a role in those diseases. Those claims are justifiable, we believe, on the basis that the inhibitor allows the test of the hypothesis and could be the actual

product if the hypothesis is correct; also, the field would be open for competitors to make other, possibly better, inhibitors as competing drugs. Claims to all possible inhibitors of the ligase would not be allowed, so no unacceptable monopoly situation would be created. The analogy in chemical patenting to claims for a new gene based on sequence similarity would be a subsequent filing on a compound, similar in chemical structure to a patented ligase inhibitor, and claiming that it was, on that basis only, probably a ligase inhibitor.

We have focused our comments on human genes. We believe that similar considerations should apply to genes from other organisms as well. For example, patent protection of entire genomes of organisms could have a devastating untoward impact on biomedical research: genome patents would provide an unacceptable monopoly that neither teaches nor enables discoveries that would promote human health and well-being.

We hope that you will accept the arguments that we have set forth and that the spirit of what we hope to achieve can guide you when considering the claims structure of patent applications for genes and especially for human genes.

Sincerely yours,

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