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Jordan J. Cohen, M.D., President

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Box Comments
Assistant Commissioner for Patents
Washington, D.C. 20231
Attention: Linda S. Therkorn

Re: Revised Interim[1] Utility Examination Guidelines [64 FR 71440], and Revised Interim Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, ¶ 1 "Written Description" Requirement [64 FR 71427].

I am writing as the President of the Association of American Medical Colleges (AAMC), representing the nation's 125 medical schools, some 400 teaching hospitals, and 91 academic medical societies. Our institutions, at which approximately half of all extramural research sponsored by the National Institutes of Health (NIH) is performed, play a central role in the Human Genome Project, including serving as host to numerous genome centers and home to thousands of contributing investigators. Medical schools and teaching hospitals also collaborate with industry in the development of new drugs, diagnostics, and innovative clinical procedures that integrate the outcomes of genomic research into medical practice. Many of these institutions are represented within the files of the Patent and Trademark Office (PTO).

A central concern to the biomedical research community is the extent to which claims on DNA, or *polynucleotide*, sequences are recognized within the patent system. In particular, the AAMC generally opposes the issuance of patents pertaining to incompletely sequenced genes or those of unknown function, as in the case of expressed sequence tags (ESTs). The principle use of ESTs is as a research tool for identifying unknown genes of yet-to-be-determined sequence and function. As in the case of other research tools, the issuance of patents on ESTs threatens to subject researchers to numerous and onerous restrictions in their ability to use or apply information entangled by these "inventions," and consequently would impede the progress of this important area of research. The posited use of ESTs for *real world* applications in forensics, gene mapping, or other areas almost always requires significant further research to enable a person of "ordinary skill in the art" to use such inventions. Moreover, a profusion of EST patents will effectively discourage researchers from determining full-length expressed and genomic sequences and isolating the protein(s) encoded by the gene for medical application for fear that success in this endeavor would plunge them into a morass of infringement claims and engender protracted litigation.

From this perspective, the AAMC has closely reviewed the above referenced interim guidelines and their implications for genomic research. In general, these guidelines make significant strides toward addressing our concerns.

Our specific comments are noted below:

- **Revised Utility Guidelines:** The AAMC commends the PTO for establishing a standard of "specific, substantial, and credible" utility in its revised guidelines. We agree that applicants for claims to expressed sequence tags, single nucleotide polymorphisms, and other gene fragments must demonstrate such utility, or their applications should be rejected.

  The AAMC strongly agrees with the NIH, representing the Public Health Service, that the revised standard should not be interpreted to embrace claims of a "theoretical function" for polynucleotide sequences, such as a homological description, as a sole basis for utility.[2] Automated programs and databases frequently enable researchers to infer, or "guess," the identity and function of a protein encoded by a gene based on the similarity of a fragment to other known genes. Such suppositions of utility are technology driven, require little scientific insight or creativity, and do not characterize a specific, substantial and credible utility.

  The guidelines provide that an examiner should not reject an application that is judged to have a *well-established* utility, regardless of the quality of the assertion made by the applicant. The PTO defines a utility as well established if a person of ordinary skill in the art would immediately appreciate that the invention would be useful based on its applications and other characteristics. It implicitly follows from the guidelines that a utility determined to be well established should also meet the standard of "specific and substantial" if an examiner decides not to impose a rejection. The AAMC believes that, in instances where the examiner perceives an invention to have a well-established utility not explicitly asserted by the applicant, the written record should clearly identify this utility and the rationale for considering it specific and substantial. A clear explication in the record will be invaluable as arguments regarding the utility of polynucleotide sequences inevitably arise in the future.

- **Revised Written Description Guidelines**: The guidance of the Court of Appeals Federal Circuit (CAFC), most recently in *Regents of the University of California v. Eli Lilly and Co.* (1997), has established the requirement that claimed DNA sequences be identified by specific formulation, as with claims on other chemical formulae. Several public comments in response to the earlier proposed written description guidelines argued that the inclusion of *open-ended claim language* in EST claims would be contrary to the CAFC's decision in *Lilly*, because a sequence described by such language would not constitute a "substantial portion of the genus." In its response, reported within the revised interim written description guidelines, the PTO has indicated that it would recognize open claim language on a gene fragment. The AAMC strongly opposes the inclusion of open claim language for an EST or other gene fragment within the written description, and agrees with the NIH's analysis that it could assist holders of such patents to assert domination over later discovered full length genes. Consequently, we urge the PTO to limit the breadth of

such claims to a scope commensurate with the sequence structure actually disclosed by the applicant.

In conclusion, the AAMC acknowledges that the patent system is a cornerstone of recent advancements in pharmaceuticals and other products that have markedly improved medical care and human health. But we also wish to stress that this progress has been built upon open scientific discovery and communication. The Association is deeply concerned about and strongly opposed to the practice of awarding broad-reaching patents on claims to DNA sequences that do not meet a rigorous, high standard of specific, substantial, and credible utility. We believe that the overly facile issuance of such patents in recent years is inimical to the progress of science, as well as to the practice of medicine, and not in the public's best interest. Therefore, we urge that the utility and written description guidelines be further strengthened and delimited, as recommended by the NIH.

Sincerely,

Jordan J. Cohen, M.D.

[1] As corrected 65 FR 3425.
[2] Letter of Harold Varmus, M.D. and Francis Collins, M.D. to Commissioner Q. Todd Dickinson, December 21, 1999.