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Submitted by email to mccuepat@mail.nih.gov

Dear Dr. McCue,

Introduction

The American Society for Clinical Pathology (ASCP), the Association for Molecular Pathology (AMP), and the College of American Pathologists (CAP) are pleased to provide comments to the National Institutes of Health in response to its October 21, 2011 Federal Register notice entitled, "Prospective Grant of Exclusive License: The Development of a Companion Diagnostic Kit for Predicting Therapeutic Efficacy of Anti-Cancer Agents." Our professional associations represent more than 120,000 physicians, doctoral scientists, and medical technologists who perform clinical laboratory testing. Our members are dedicated to the development and implementation of pathology testing for the benefit of our patients in a manner consistent with the highest standards established by the Clinical Laboratory Improvement Amendments (CLIA), the College of American Pathologists (CAP), the American College of Medical Genetics (ACMG), and the Food & Drug Administration (FDA). Our members develop, implement, interpret, and provide consultation regarding tests, both routine and novel, that are used for diagnosis, prognosis and patient management in all medical areas including cancer, infectious diseases, heritable disorders, and histocompatibility testing.

ASCP, AMP, and CAP oppose and object to the grant of an exclusive license on U.S. Patent Application 61/144,501 for the reasons outlined below.

I. U.S. Patent Application 61/144,501 fails to meet the conditions for an exclusive license of a federally-owned invention.

The conditions that must be satisfied to allow for exclusive licensing of a federally-owned invention are set forth in 35 U.S.C. 209(a) and 37 C.F.R. 404.7. According to the National Institutes of Health Office of Technology Transfer, under 37 C.F.R. 404.7 exclusive licensing

(1) must serve the best interests of the public;

(2) practical application of the invention must be unlikely under a nonexclusive license;

(3) an exclusive license must be a reasonable and necessary incentive for the investment of capital, and required to bring the invention to practical application; (4) the scope of exclusivity cannot be broader than necessary to bring the invention to practical application; and

(5) exclusive licensing must not lessen competition.

Patent application 61/144,501, and any and all subsets of the individual proteins and tumors specified therein, fail to meet these stated preconditions for an exclusive license. First, the patent claims as a process the simple act of quantifying two or more of many known cancer related proteins, without specifying any particular method, and after a standard normalization calculation that is typically required by a quantitative technique, comparing the respective normalized protein levels and correlating the results with prognosis for essentially all human cancers.

On its face, this patent application is so broad as to encompass essentially all techniques of quantifying proteins in tissue, blood and body fluids required for making use of the information in a medically meaningful way. This monopolization of an incalculable number of biological relationships between relative protein expression levels and cancer prognosis is absolutely, unequivocally adverse to the public interest because it would place a virtually unlimited swathe of protein diagnostics under the control of a single entity, dramatically inhibiting the growth of potential diagnostic assays and methods. Moreover, exclusively licensing the relationships within the submitted patent application would substantially increase the costs of, and decrease patient access to those tests that do manage to enter medical practice. It logically follows from this rationale that an exclusive license of the right to quantify, compare, and correlate a limited number of proteins for a restricted group of cancer types is similarly undesirable and impermissible because of the absolute monopolies it would confer for each set of quantitative protein–cancer relationships. A license of this nature would diminish the incentives for innovation in assay development and methods of quantitation, and reduce patient access to testing.

Because of patent application 61/144,501's breadth, its utter lack of novelty, and the sheer obviousness of the patent application's claims, it is extraordinarily difficult to argue that practical application of any of the claimed biological relationships is unlikely without an exclusive license, or that an exclusive license is reasonable and necessary for medical use of the aforesaid natural phenomena. As has been described, its breadth renders patent application 61/155,501 unusually unsuitable for an exclusive license. Finally, an exclusive license of any of the biological relationships within this patent is certain to decrease, rather than increase competition.

II. An exclusive license would give a single company monopolistic control over clinical testing for key biological relationships in cancer.

Patent application 61/144,501 claims as an invention the comparison of the expression levels of two or more of many specified proteins the expression of which has long been known to be altered in malignant tumors. The patent application fails to specify particular methods of measurement of protein expression levels, thus claiming any and all uses of the aforementioned biological relationships. By granting an exclusive license for any of the quantitative protein-cancer relationships claimed in this patent application, NIH would, if the patent is awarded, be granting to a sole corporate entity the right to exclude all others from performing medical testing for key biological relationships that are central to the oncologic process, thereby stifling the practice of medicine. Because of the patent application's breadth and the nature of the biological relationships, it is unlikely or impossible for one to invent around the patent claims. Therefore, an exclusive patent license is likely to result in monopolistic pricing and substantial patient harms resulting from cost-based limitations in patent access. Further, the lack of competitive pressure will result in decreased innovation in the development of actual test methods for measuring the protein expression levels granted in an exclusive license.

III. The proposed sub-licensing requirement for confirmatory testing does not ensure patient access to alternative testing.

We have been informed that NIH will require the applicant for an exclusive license on patent application 61/144,501 to offer sublicenses for confirmatory testing. Patent application 61/144,501 does not meet the conditions for an exclusive license of a federal invention. However, even if this patent application did satisfy the criteria for an exclusive license, mandatory sublicensing alone would be insufficient to ensure patient access to alternative testing. First, in order to have a possibility of making useful confirmatory testing available to patients, sublicenses would need to guarantee the right to examine the claimed biological relationships using any test method. Result confirmation with the same test sold by the patent applicant in kit form would be unlikely to uncover methodologic flaws or idiosyncratic performance issues in particular patients. Conversely, the limited volumes associated with confirmatory testing would probably be viewed as inadequate to support the investment necessary to design, optimize, and validate another test. Thus, mandatory sublicenses alone will not solve problems of patient access posed by an exclusive license, even within the limited realm of confirmatory testing.

IV. Many of the claims in U.S. Patent Application 61/144,501 are invalid under 35 U.S.C. §§ 101, 102, 103 and 114.

Patent application 61/144,501 contains a number of claims which are neither novel nor non-obvious under 35 U.S.C. §§ 102 and 103, fail to meet the written description requirements of 35 U.S.C. § 114, and impermissibly claim natural laws and or phenomena under 35 U.S.C. § 101. First, protein measurement has long been utilized in clinical diagnostics, and is a fertile area of research, including the application of quantitative image analysis techniques to visually determine protein expression levels. The use of normalization is a standard, frequently essential technique that is commonly applied prior to the comparison of empirically derived numerical values. The existence of biological relationships between relative protein expression levels in cancer and clinical characteristics such as prognosis or drug responsiveness is obvious and well-known, and in fact forms the basis of what many think of as "personalized medicine" in cancer. Thus, the measurement of protein levels and describing clinical relationships stemming therefrom is not new or novel, and is in fact obvious. Moreover, because it merely frames these biological relationships as processes as a means of claiming the relationships themselves, the patent application is invalid under 35 U.S.C. § 101. Further, because application 62/144,501 claims many if not all methods of measuring protein expression levels without directly specifying them, it fails to meet the written description demanded by 35 U.S.C. § 114. Finally, although the patent application claims membrane based steps prior to measuring protein levels, membrane transfer has long been used in protein and molecular biology research and clinical diagnostics, as evidenced, for example, by the ubiquitous "Southern blot" (DNA), "northern blot" (RNA), and western blot (protein), rendering the related claims neither novel nor nonobvious.

V. Conclusion

Thank you very much for the opportunity to provide comments on NIH's "Prospective Grant of Exclusive License: The Development of a Companion Diagnostic Kit for Predicting Therapeutic Efficacy of Anti-Cancer Agents." As a general principle, our organizations oppose exclusive licensing of patents on governmental inventions that do not clearly advance the public interest. Such licenses, in the rare circumstances in which they are granted, should be narrowly targeted and not extend further

than is necessary to encourage commercialization. Moreover, for inventions in which clinical laboratory testing is potentially impacted, sublicenses for confirmatory testing that include reasonable royalty rates and the right to use alternative test methodologies should be mandated. For the aforementioned reasons, the patent application at issue fails to meet NIH's stated burdens. We offer our assistance to the Agency as you address this important issue, and looks forward to further discussions with you.

Thank you for your consideration of this request. If you need additional information, please contact Mary Williams, Executive Director of AMP, at mwilliams@amp.org or (301)634-7921.

Sincerely,
American Society for Clinical Pathology
Association for Molecular Pathology
College of American Pathologists