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Sent: Monday, July 21, 2014 2:23 PM
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Subject: ASP response

Please find attached a letter from the American Society of Pharmacognosy in regards to the Request for Written Comments on Guidance for Determining Subject Matter Eligibility of Claims Reciting or Involving Laws of Nature, Natural Phenomena, & Natural Products.

Thank you for allowing us the opportunity to respond to this very important guidance memorandum.

Sincerely,

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DATE: July 21, 2014

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FROM: American Society of Pharmacognosy (ASP), Officers and Executive Committee

SUBJECT: **Response to Request for Written Comments on Guidance for Determining Subject Matter Eligibility of Claims Reciting or Involving Laws of Nature, Natural Phenomena, & Natural Products**

Dear Commissioner,

The Officers and Executive Committee of the American Society of Pharmacognosy (ASP) desires to offer comments in response to the Request for Written Comments on the USPTO Guidance for examining patent applications involving natural products. We are greatly concerned about the potential negative impacts associated with the new guidance "*2014 Procedure for Subject Matter Eligibility Analysis of Claims Reciting or Involving Laws of Nature/Natural Principles, Natural Phenomena and/or Natural Products.*"

Introduction and General Remarks

The American Society of Pharmacognosy (ASP) is the premier organization of scientists specializing in the isolation and characterization of natural product chemicals in the United States. The purpose of the ASP is to unite international scholars in their quests: "to promote the growth and development of pharmacognosy (the study of medicines from natural sources), to provide the opportunity for association among the workers in that science and in related sciences, to provide opportunities for presentation of research achievements, and to promote the publication of meritorious research."

Inventions capitalizing on natural products are pivotal to scholarly development and to advances in the US biopharmaceutical industry. Thus, in view of the Supreme Court's decision in *Myriad* (2013) and *Mayo* (2012) cases, the officers and executive committee of the ASP feel obligated to comment publicly on the proposed interpretation of the USPTO Guidance of March 4, 2014. For more than 50 years, the members of ASP have been able to extend the impact of their academic research through collaborations with the biopharmaceutical industry. Similarly, creative compositions derived from naturally occurring small molecules have long been a mainstay of the US biopharmaceutical industry, with advances largely stimulated by the ability to pursue patents. Many therapeutic compositions are derived from natural products and they are disproportionately used to treat high-need diseases, such as viral infections, bacterial diseases and to battle cancer. The

ASP is convinced that natural product-related drug development is likely to grow in importance in the coming years, as recent advances in related fields have made it possible to access large reserves of natural products that were previously unavailable. Therefore, it is important not to unduly restrict the scope of patentable subject matter with respect to innovations relating to or derived from natural products.

Some Important Historical Perspectives Based on Patented Natural Products

More than 200 years ago, the first pharmacologically active pure compound, morphine, was isolated from seed pods of the opium poppy. In the early 20th century important antibiotics were discovered, headed by penicillin and other natural products such as tetracycline and erythromycin. These and other compositions derived from naturally occurring small molecules have played a central role in the development of effective drugs, in part because of USPTO issued patents. These patents, as well as others relating to innovative compositions containing naturally occurring compounds and their purification, have played a key role in launching the US biopharmaceutical industry and has led to countless advances in medicinal science. Overall, up to this point in US history, we have benefited from an era wherein drugs from nature could be purified, studied, and developed into life-saving medicines.

Natural Products and Medicines

ASP is concerned that the present interpretation of the Guidance may have the inadvertent outcome of hindering the development of new medicines. It must be noted that natural product drugs helped create the modern pharmaceutical industry that has provided humankind with a large number of life-saving medicines. Natural products have been, and continue to be, an invaluable source of novel drug compositions for the treatment of many diseases. Of the 1073 small molecules approved as drugs between 1981 and 2010, 59 (6%) are compositions containing natural products. Another 299 (28%) are derived from natural products, 177 (16%) are synthetic structures that are derived directly from natural products, and 146 (14%) are synthetic structures that are modeled on a natural product (David J. Newman and Gordon M. Cragg, "Natural Products as Sources of New Drugs over the 30 Years from 1981 to 2010", *Journal of Natural Products*, 2012; 75(3), 311-335). Only 36% of all approved drugs during this time frame are purely synthetic structures that were derived without reliance on natural products. In the case of anti-infective drugs, approximately 70% of clinically used antibiotics are natural products. With the serious emergence of antibiotic-resistant pathogenic bacteria, it is critical that we continue to develop new antibiotic drugs to effectively and safely combat bacterial diseases. With nature's impressive record for providing important drugs to treat human bacterial pathogens, it is important that we continue to search for new cures from natural resources. That search will be significantly hampered by the current USPTO Guidance and will impede future drug discovery and development.

Natural Product "Amazonic Acid" – Structure and Function

The USPTO draft Guidance suggests that the isolation, structure elucidation, physical characterization and identification of a novel use of a natural product is an insufficient "hand-of-man" contribution to merit patent eligibility. In particular, the USPTO Guidance uses the example of "amazonic acid", a hypothetical natural product with anti-cancer activity, as an example of a substance that does not qualify for patent protection, as it is not "substantially different" from the "amazonic acid" found in nature. We disagree. In this hypothetical case, the natural biological role of "amazonic acid" in the plant has a defined function, which is not to cure cancer in humans. Further, the natural product in the tree leaf is present in such trace amounts that in order to be "to be effective, a patient must eat 30 pounds of the leaves per day". Accordingly, by way of the isolation,

structure elucidation, physical characterization and identification of a novel use, a "new and useful … composition of matter" has been demonstrated. Since at least the 1940s, the USPTO has been granting patents on inventions relating to naturally occurring small molecules (e.g., antibiotics streptomycin and actinomycin). These patents have dealt with inventive processes for producing the molecules and compositions of the molecules derived from nature. Significantly, courts have also recognized that compositions containing naturally occurring small molecules (similar to the amazonic acid in the USPTO Guidance's Example B) may be patentable subject matter. We believe that the Supreme Court's analysis in *Myriad* with respect to isolated DNA is limiting, and not reflective of all situations involving small-molecule natural products as therapeutic entities.

The 2014 Restrictions Will Hinder Drug Development

It is important to further underscore key points summarized above. In 2003, the FDA approved daptomycin for specific microbial infections. Daptomycin is a natural product, which has since spawned a number of chemical modifications. However, none of this would have been possible if the original structure of the natural product daptomycin (from nature) had not been patent-eligible. Very recently, dalbavancin was approved for specific bacterial infections. Again, dalbavancin would never have been developed if the parent compound, the major antibiotic vancomycin, had not been patentable 50 years ago. We therefore respectfully request that the USPTO Guidance be revised to give weight to the very substantial inventive contribution of natural product scientists in the isolation, molecular characterization, and pharmacological characterization of novel chemical entities derived from natural organisms. We assert that the association of a novel bioactivity with a previously unknown discrete chemical entity derived from a natural source should be sufficient evidence of the "hand-of-man" to allow composition of matter claims based on its chemical structure and the associated biological activity. We believe that such an interpretation will be consistent with the Supreme Court decision by limiting the broad claims associated with patents on genes as in *Myriad* while still allowing for discrete composition of matter claims on bioactive natural product chemicals.

Sincerely,

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