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Mr. Andrew H. Hirshfeld
Deputy Commissioner for Patent Examination Policy
United States Patent and Trademark Office
P.O. Box 1450
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Comments of Warp Drive Bio in Response to the USPTO's Guidance For Determining Subject Matter Eligibility of Claims Reciting or Involving Laws of Nature, Natural Phenomena & Natural Products

Dear Mr. Hirshfeld:

We thank the U.S. Patent and Trademark Office (USPTO) for the opportunity to submit comments on the Guidance for Determining Subject Matter Eligibility of Claims Reciting or Involving Laws of Nature, Natural Phenomena & Natural Products ("the Guidance document"). We appreciate the efforts being made by the USPTO to provide guidance to its patent examiners so that patent claims are examined in a consistent and uniform manner. We are concerned, however, that the Guidance document oversimplifies the determination of what qualifies as patent-eligible subject matter and in the process sweeps into the excluded category inventions that rightfully should be considered patent-eligible. We are similarly concerned that the Guidance document does not set forth which party (the patent examiner or the applicant) has the initial burden of demonstrating that the claimed subject matter is or is not patent-eligible. We request that the USPTO consider providing guidance to its patent examiners regarding (i) what constitutes a "natural product" and (ii) which party has the burden of establishing whether a claimed compound is a "natural product."

The Guidance Document Does Not Define "Natural Product"

In the Guidance document, the USPTO provides a flowchart of three questions to assist patent examiners in determining whether a claim is drawn to patent-eligible subject matter. The second question asks, "[d]oes the claim recite or involve judicial exception(s)?" One judicial exception called out in the flowchart is the category of "natural products." Unfortunately, the Guidance document does not clearly articulate what qualifies as a natural product. As discussed below, under certain circumstances it may be difficult or even impossible to determine whether a given compound is a natural product.

We propose that the term "natural product," as used in the Guidelines, refer to a compound that is known to exist in nature. Organisms from bacteria and fungi to higher plants and animals produce diverse compounds as part of their natural biology. For example, the drug Paclitaxel is produced by the Pacific yew tree in its natural environment. Without assenting to the USPTO's view that claims to such products, in isolated form, are not patent-eligible, we agree that compounds of this type are generally accepted by the scientific community as being natural products because they have been identified as being present in the natural environment.

It is important to recognize, however, that certain organisms are capable of producing compounds in artificial settings that they may never produce in nature. For example, if an antibody is raised in a rabbit against a novel antigen that the rabbit does not encounter in nature, then that antibody is presumably novel. While the antibody is produced by a natural organism, the antibody itself would be considered patent-eligible.[1] Therefore, the mere fact that a compound is produced by a natural organism is not sufficient justification to classify that compound as a natural product; rather, the compound must be produced by the natural organism in the natural environment. Conversely, if the compound is produced by the organism under artificial conditions, it cannot *prima facie* be concluded that the compound is a natural product.

To consider a second example, bacterial strains grown under artificial culture conditions in a laboratory setting can produce a variety of compounds. Furthermore, the specific compound(s) produced depends on the specific artificial culture conditions and under some culture conditions particular compounds may not be produced at detectable levels at all. The ability of a bacterial strain to produce a compound under artificial conditions does not *prima facie* indicate that the strain produces the same compound in its natural environment. Complicating the matter further, some bacterial strains may only produce certain compounds when artificial regulatory sequences are inserted into the bacterial genome. Again, the ability of a bacterial strain to produce a compound under artificial conditions does not prove that the strain produces the same compound in its natural environment. For these reasons, if a compound is produced by an organism in an artificial context or environment and is not known to exist in nature, the compound should not, for the purposes of determining patent eligibility, be considered a "natural product."

[1] Claims directed to novel antibodies have long been recognized as being patent-eligible subject matter, and we do not read the Guidelines document as indicating a shift in the USPTO's views on that subject. In contrast, a claim to a purified preparation of a naturally-occurring antibody would not be patent-eligible under the Guidance document.

A compound conceived and synthesized entirely by mankind could in principle also occur in nature at the time of the invention of the compound. Indeed, there are a number of documented examples of compounds that were first conceived and synthesized by mankind and later discovered to exist in nature, including Tramadol, 5-deazariboflavin, and phosphonoformate. The first synthesis of Tramadol was reported in 1965. A composition of matter patent was granted by the USPTO in 1972 (U.S. Pat. No. 3,652,589). Tramadol was approved by the FDA in 1995and is now marketed worldwide. Yet, four decades after the patent was issued, Boumendjiel et al. (2013) isolated Tramadol from the bark of the African peach tree (*Angew. Chem. Int. Ed.* 2013, 52:11780-11784).

We submit that compounds produced by organisms under artificial conditions and which have not been identified in nature should be treated in the same manner as synthetically produced compounds such as Tramadol. As is discussed above, the fact that a compound can be produced by an organism under artificial conditions does not prove that the compound is produced by that organism in nature. At best, in the absence of evidence in the scientific literature, the examiner would only be able to conclude that the compound *might* occur in the natural environment. Yet, in discussing a particular hypothetical molecule that might exist in nature, the Supreme Court in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. __, 133, stated: "The possibility that an unusual and rare phenomenon *might* randomly create a molecule similar to one created synthetically through human ingenuity does not render a composition of matter nonpatentable." A fair reading of this passage suggests that a patent examiner presented with a situation involving a claimed composition that *might* exist in nature should consider the claim patent-eligible. In addition to failing to present a *prima facie* case of unpatentability in the absence of evidence showing the existence of a claimed composition in nature, the Supreme Court has indicated that the possibility that a compound might exist in nature "does not render a composition of matter unpatentable." In light of this, we propose that the term "natural product" as used in the Guidelines, refer to a compound that is known to exist in nature. We further propose that the Guidance document be revised to remind the patent examiners that there is a distinction between a natural product and a product that is produced by a natural organism, which may or may not be a natural product.

The Guidance Document Does Not Adequately Set Forth the Examiner's Burden of Demonstrating that a Compound is a Natural Product

Just as it does not place the burden on applicants to demonstrate novelty and non-obviousness, it is clear the USPTO should not ask all applicants to demonstrate that a claimed compound does not occur in nature—that burden of proof would be impossible to meet. Rather, as with novelty and non-obviousness, the Examiner should bear the initial burden of presenting a *prima facie* case of unpatentability.

Unfortunately, the Guidance document does not discuss either the Examiner's initial burden or the Supreme Court's rejection of a probabilistic-based patent-eligibility determination. The Guidance document flowchart sets forth a sequence of questions to be posed by the Examiner. If the answer to question 2 ("Does the claim recite or involve judicial exception(s)?") is "no," then the claim qualifies as patent-eligible subject matter. If, however, it is unclear whether the claim recites or involves a judicial exception such as a natural product, the claim may or may not qualify as patent-eligible subject matter. The flowchart provides limited additional guidance. We propose that the Guidelines document be revised to clarify that the initial burden of presenting a *prima facie* case that a compound is a natural product is borne by the examiner, and that the mere possibility that a compound is naturally occurring is not sufficient to shift the burden to the applicant.

Conclusion

We propose that the term "natural product" as used in the Guidelines, refer to a compound that is known to exist in nature. If a compound is produced by a natural organism in an artificial environment and is not known to be produced in nature, the compound should not be considered a "natural product." We further propose that the examiner bears the initial burden of presenting a *prima facie* case that a compound is a natural product. That a compound might exist in nature is not sufficient to shift the burden to the applicant.

We appreciate the efforts being made by the USPTO to provide guidance to its patent examiners so that patent claims are examined in a consistent and uniform manner and we thank the USPTO for its public outreach soliciting feedback on the Guidance document.

Respectfully submitted,

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