81(200) FR 71487 (2016) Roundtable 1

Dear Honorable Commissioner

I write herein to provide comments the May 2016 Life Sciences examples.

A focus on "directed to" would be more logical.

The new Guidance is helpful in-so-much as it provides a pathway to avoid some of the 101 ineligibility results, but it propagates certain mistakes from Mayo and Myriad, leading to artificial drafting efforts, divorcing claims from the real life context of an invention, and I believe we can do better.

For example, the Julitis claim 1 example provides that "detection" methods without conclusions are not "directed to" a judicial exception. This example indicates that practitioners with diagnostic inventions need simply sidestep "diagnostic" language and avoid stating any medical relevant conclusions. Similarly, hybridization claim 75 indicates that divorcing the claim from the medical reason for performing the test and from the DNA itself, is sufficient to avoid the toxic effect of referencing a judicial exception in the claim.

Of course, such claims may well fail novelty tests if the relevant protein or DNA was already known and subject to various detection methods, so while **seeming** to provide some relief, in most cases it will not be possible to obtain such claims.

Further, the analysis of Julitis claim 2 is illogical—silly even—because substantively, claims 1 and 2 read on the **same** activities. Whether the conclusion is recited in the claim or not, it is inherently going to be made.

To provide another example, if Edison had had the misfortune to recite in his lightbulb patent claim that increasing current or voltage would make the bulb brighter, the recitation of such a natural law would poison the entire claim under this approach. Hence, the light bulb would no longer be patent eligible under the proposed framework. Yet, whether recited or not, the light bulb must necessarily function in accordance with the natural law—that's why we refer to them as laws.

Claim 3 of the Julitis example clarifies that one can also get around Mayo/Myriad by reciting technical specifics. Thus, with a plurality of claims, one can get all possible means of performing the same assay as recited in claim 2. It will, of course, cost more and lead to claim proliferation—neither of which will increase access to health care.

It would be less logically strained to focus instead on the "directed to" language. Julitis claim 2 recites a biological correlation, but it is not "directed to" that correlation. Rather, it is directed to a medical test that just happens to **use** the correlation.

We can tell the difference, because no person with Jul-1 antibodies in their plasma infringes the claim. No sample of plasma with JUL-1 antibodies infringes the claim. No person diagnosed with Julitis infringes the claim. Indeed, no prior methods of diagnosing Julitis infringe the claim. Of course not, because the claim isn't "directed to" the natural correlation between JUL-1 levels and the Julitis. It only **uses** that correlation in a diagnostic test.

Mayo should be limited to its narrow facts—a case where the claim was already anticipated, and reciting the correlation made no **active** difference in the claim. Recall there was no "change the dosage" completion step and the only two active verbs were already long in the art. Indeed, the claim **as a whole** in Mayo was **routine** and conventional. *See e.g., Rapid Litigation Management Ltd v. CellzDirect, Inc*. 827 F.3d 1042, 1051(Fed. Cir. 2016) ("in examining claims under step two [of the patent eligibility analysis], we must view them **as a whole**, considering their elements "both individually and 'as an ordered combination.' Alice, 134 S. Ct. at 2355 (quoting Mayo, 132 S. Ct. at 1298).") (emphasis added). The new language related to the metabolite levels that were too high or low, failed to include any active steps, and was inherent to the prior art, even if previously unknown.

Purified natural products are often significantly different from products in nature

I also would note with respect to claim 3 of the vaccine example that peptide F as it exists in nature cannot be used as a vaccine, whereas the claimed peptide F[1] plus water can be.

[1] The peptide should be expressly limited to "purified" Peptide F, but that is true for the other claims as well, lest e.g., Claim 2 read on cooked pigeons.

Thus, it is indeed significantly changed from its natural counterpart, which causes infection, thus preventing use as a vaccine. Peptide F by itself has an entirely new medical functionality, not possible with the natural form of the virus.

Failure to recognize this relegates many natural products to languish without the patent protection needed to encourage development funding. Since some 30-40% of our drugs are still natural products or derived therefrom, this will have significant negative impact.[2]

In fact, most natural products have significant medical functionality not possible with the natural form of the product.

Adrenaline is a good example. It was probably the first human hormone patented in 1906 in its purified form.[3] Adrenaline—also known as epinephrine—has saved countless lives and is still in use today. Indeed, many people carry an Epipen® and can testify to its life saving capabilities in the event of anaphylaxis.

The original adrenaline patent did **not** cover adrenaline in its natural form as found in a human being or animal. That could not be patented because it was not new. Instead, the patent only covered the **purified** form of the hormone, which at that time was new.[4]

In fact, Judge Learned Hand noted that the inventor "was the first to make it available for any use by removing it from the other gland-tissue in which it was found, and, while it is of course possible logically to call this a purification of the principle, it **became for every practical purpose a new thing commercially and therapeutically. That was a good ground for a patent**."[5] Thus, Learned Hand recognized that adrenaline as found in an animal's glandular tissue had virtually no therapeutic use due to the low concentration and impurities, whereas the purified adrenaline had therapeutic (and commercial) value.

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[2] David J. Newman & Gordon M. Cragg , Natural Products As Sources of New Drugs over the 30 Years from 1981 to 2010. J. Natural Prod. 75:311-335 (2012). See e.g., FIG. 5.

[3] *See* US730176 (1. A substance possessing the herein-described physiological characteristics and reactions of the suprarenal glands in a stable and concentrated form, and practically free from inert and associated gland-tissue.").

[4] *Id.*

[5] *Parke-Davis & Co. v. H. K. Mulford Co.*, 189 F. 95, 103 (C.C.S.D.N.Y. 1911) (the cited quote was arguably only dicta, but the analysis was correct).

Insulin is another good example of a life saving natural product. It was first patented when Banting partially purified it from dog pancreas[6] and has saved countless lives since. One could treat diabetes by eating raw pancreas,[7] but that isn't very practical in the event of diabetic coma. Thus, the discovery of at least partially purified insulin was a great therapeutic benefit to patients.

Vitamin B12 is another natural compound patented in purified form.[8] Prior to the patent, anemia was treated by eating raw liver, and thus the discovery of purified B12 was great medical advance over consuming large quantities of raw liver.[9]

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[6] *See* US1469994, Extract obtainable from the mammalian pancreas or from the related glands in fishes, useful in the treatment of diabetes mellitus, and a method of preparing it. Claim 1: "A substance prepared from fresh pancreatic or related glands containing in concentrated form the ductless portion of the glands sufficiently free from injurious substances for repeated administration and having a physiological characteristics of causing a reduction in blood sugar useful for the treatment of diabetes mellitus."

[7] George Graham G., Treatment Of Diabetes By Raw Fresh Gland (Pancreas), Br Med J. 1(3357): 859–860 (1925).

[8] US2563794 ("The compound vitamin B12 an organic substance containing cobalt, together with carbon, nitrogen, hydrogen, oxygen, and phosphorus, said compound being a red crystalline substance soluble in water, methyl and ethyl alcohol and phenol, and insoluble in acetone, ether and chloroform, and exhibiting strong absorption maxima at about 2780 A 3610 A. and 5500 5., and an L. L. D. activity of about 11,000,000 L. L. D. units per milligram."). *See also Merck & Co. v. Olin Mathieson Chem. Corp*., 253 F.2d 156 (4th Cir. 1958) (upholding Vitamin B12 patent US2703302 and stating "The patentees have given us for the first time a medicine which can be used successfully in the treatment of pernicious anemia, a medicine which avoids the dangers and disadvantages of the liver extracts, the only remedies available prior to this invention, a medicine subject to accurate standardization and which can be produced in large quantities and inexpensively, a medicine which is valuable for other purposes, as well as for the treatment of pernicious anemia. It did not exist in nature in the form in which the patentees produced it and was produced by them only after lengthy experiments. Nothing in the prior art either anticipated or suggested it.").

[9] Whipple G.H. & Robscheit-Robbins F.S., Favourable influence of liver, heart and skeletal muscle in diet on blood regeneration in anemia. Am J Physiol. 1925; 72:408–18. Indeed, George Hoyt Whipple shared the 1934 Nobel Prize in Medicine with 1934 with George Richards Minot, and William Parry Murphy "for their discoveries concerning liver therapy in cases of anemia."

Even DNA has significant medical use when purified. Before any DNA is purified and sequenced it cannot be used in any diagnostic method. Indeed, before whole genome sequencing was invented no gene diagnostics could be performed without a small piece of purified DNA. Thus, at the time even DNA had significant medical uses not possible on DNA in its natural form.

While the Supreme Court came to the opposite conclusion, the Constitution is the higher law. Article 1, Section 8 of the Constitution of the United States of America, gives congress certain powers, including the power "To promote the progress of science and useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings **and discoveries**…" Thus, the Supreme Court's holding regarding the ineligibility of DNA for patent is arguably unconstitutional. *Assoc. Mol. Pathology v. Myriad Genetics, Inc.,* 569 U.S._, slip op. at 12 (2013) ("Groundbreaking, innovative, or even brilliant discovery does not by itself satisfy the §101 inquiry.").

Thank you for your time, attention and efforts. Rest assured that in spite of the criticisms raised here, I recognize that current 101 morass is not the PTO's fault.

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P.S. Please stop repeating that a biological correlation is a natural law. It was embarrassing when Justice Breyer said it, and those of us with scientific training should not repeat it. F = MA is a natural law, and there is no "law" in any biological correlation. Indeed, every human processes drugs at ***different*** *rates, which is why finding the medically useful metabolite range in the Mayo patent had value.*