Subject Matter Eligibility Examples: Life Sciences

The following examples should be used in conjunction with the *2014 Interim Guidance on Subject Matter Eligibility* (2014 IEG). As the examples are intended to be illustrative only, they should be interpreted based on the fact patterns set forth below. Other fact patterns may have different eligibility outcomes. While some of the fact patterns draw from U.S. Supreme Court or U.S. Court of Appeals for the Federal Circuit decisions, each of the examples shows how claims should be analyzed under the 2014 IEG. All of the claims are analyzed for eligibility in accordance with their broadest reasonable interpretation.

Note that the examples herein are numbered consecutively beginning with number 28, because 27 examples were previously issued. A comprehensive index of all examples for use with the 2014 IEG is provided in the attached appendix (which is an updated version of Appendix 2 to the July 2015 Update).

28. Vaccines

This example illustrates the application of the markedly different characteristics and significantly more analyses to claims reciting hypothetical nature-based products. It also illustrates the importance of applying the broadest reasonable interpretation in the eligibility analysis, and how that interpretation assists in the identification of appropriate naturally occurring counterparts of claimed nature-based products. Hypothetical claims 1, 2 and 4-6 are eligible in Step 2A, because the claimed nature-based products have markedly different characteristics from what exists in nature. Hypothetical claim 3 is ineligible, because the claimed nature-based product lacks markedly different characteristics from what exists in nature, and the claim fails to amount to significantly more than the exceptions. Hypothetical claim 7 is eligible in Step 2B, because although the claim is directed to an exception, it recites a particular and unconventional device that amounts to significantly more than the exception.

Background

Applicant discloses an influenza A viral strain, which was named the "Pigeon flu" because it was discovered in pigeons. Applicant filed an application disclosing several types of Pigeon flu vaccines, and evaluating their functional characteristics (such as immunogenicity) in terms of their seroprotection rate, *i.e.*, the percentage of vaccinated patients who developed immunity to the Pigeon flu. The disclosed vaccines include:

- Vaccines comprising "live attenuated Pigeon flu virus", which the specification defines as a live mutant virus that has been attenuated so that it has at least one mutation (*i.e.*, a change in the nucleotide sequence) of its polymerase gene, which reduces its virulence as compared to naturally occurring Pigeon flu virus. No mutations of this polymerase gene are known to occur in nature. Applicant created this mutant attenuated virus by isolating Pigeon flu virus from infected pigeons, and passaging the isolated virus through a cell culture at least 50 times until the desired mutation occurred. The live attenuated Pigeon flu virus is safe (unable to cause disease in pigeons or other test animals) and strongly immunogenic, *e.g.*, it has a high seroprotection rate of about 85%.
- Vaccines comprising "inactivated Pigeon flu virus", which the specification defines as a dead virus that is formalin-inactivated, *i.e.*, the naturally occurring Pigeon flu virus was contacted with a chemical solution called formalin that causes structural changes to the virus (*e.g.*, it chemically modifies the viral nucleic acids in a manner that does not occur in nature) so that it can no longer reproduce. Because the inactivated virus can no longer replicate, it is unable to cause disease in pigeons or other test animals, but it is still strongly immunogenic, *e.g.*, it has a high seroprotection rate of about 75%.

- Vaccines comprising Peptide F (a naturally occurring peptide isolated from the Pigeon flu virus) either alone or mixed with a pharmaceutically acceptable carrier such as water. Prior to applicant's invention, and at the time of filing the application, water was routinely and conventionally used as a carrier for peptide vaccines. Isolation does not change any structural or functional characteristics of Peptide F. Applicant discloses vaccines where the suitable pharmaceutically acceptable carrier is selected from a group consisting of a cream, emulsion, gel, liposome, nanoparticle, or ointment. Applicant discloses that although the carriers in this group comprise naturally occurring components (such as water and oil), when the components are assembled into the carrier form, the carrier has changed structural and physical characteristics that distinguish it from the closest counterpart in nature. *E.g.*, a pharmaceutically acceptable cream comprising water and vegetable oil has a form (a semi-solid homogeneous emulsion) that is structurally and physically distinct from the water and oil in nature. These vaccines are weakly immunogenic, *e.g.*, they have a low seroprotection rate of about 30%, meaning that many people who are vaccinated with these vaccines will not develop immunity to the Pigeon flu.
- Vaccines comprising Peptide F mixed with aluminum salt adjuvants (a well-known class of adjuvants) such as aluminum phosphate ($AlPO_4$). While many of these adjuvants including aluminum phosphate are naturally occurring, none of them occur together with Peptide F in nature. Adjuvants are commonly added to vaccines in order to improve their functional characteristics, *e.g.*, by increasing the strength of the immune response that the vaccines produce (immunogenicity). The amount of adjuvant sufficient to increase a vaccine's immunogenicity to a level high enough to effectively vaccinate a typical patient is called the "immuno-effective amount", and those skilled in the art understand that this amount may vary depending on the particular adjuvant and formulation selected. Adjuvants can increase immunogenicity in several ways, such as by slowing the release of Peptide F to tissue around the injection site, and/or by improving the delivery of Peptide F to the patient's lymph nodes. On their own or combined with water or other common carriers, Peptide F induces only a weak protective immune response to Pigeon flu virus (seroprotection rate of 30%), and the adjuvants do not induce any protective immune response to Pigeon flu virus (seroprotection rate of 0%). When immuno-effective amounts of the disclosed adjuvants are combined with Peptide F, however, the combined vaccine induces a strong immune response to Pigeon flu virus (seroprotection rate of 80%).

Applicant also discloses vaccine delivery devices comprising coated microneedle arrays for delivery of a vaccine comprising Peptide F. Prior to applicant's invention, and at the time the application was filed, it was routine and conventional in the field to use syringes, but not coated microneedle arrays, for vaccine delivery. A pre-filled syringe is a tube that has been loaded with a vaccine dose prior to distribution of the vaccine to health professionals. The syringe can be fitted with a hollow needle about 5/8" to 1.5" long to administer the vaccine subcutaneously or intramuscularly. A coated microneedle array comprises a plurality of very small solid needles (e.g., less than 0.05" long) that are coated with a vaccine formulation, which is placed against a patient's skin to administer the vaccine into the skin (transcutaneously). Because the microneedles are very small, administration of a vaccine with a microneedle array is virtually painless.

Claims

1. A vaccine comprising live attenuated Pigeon flu virus.

2. A vaccine comprising inactivated Pigeon flu virus.

3. A vaccine comprising:
   Peptide F; and
   a pharmaceutically acceptable carrier.

4. A vaccine comprising:
   Peptide F; and
   a pharmaceutically acceptable carrier selected from the group consisting of a cream, emulsion, gel, liposome, nanoparticle, or ointment.

5. A vaccine comprising:
   Peptide F; and
   an immuno-effective amount of an aluminum salt adjuvant.

6. A vaccine comprising:
   Peptide F;
   an immuno-effective amount of an aluminum salt adjuvant; and
   a pharmaceutically acceptable carrier.

7. A vaccine delivery device comprising a microneedle array that is coated with a vaccine comprising Peptide F.

Analysis

Claim 1: Eligible.

The claim recites a vaccine comprising live attenuated Pigeon flu virus. Based on the plain meaning of "vaccine", and the specification's definition of "live attenuated Pigeon flu virus", the broadest reasonable interpretation of the claim is live mutant Pigeon flu virus that has been attenuated so that it has at least one mutation (*i.e.*, a change in its nucleotide sequence) that reduces its virulence as compared to naturally occurring Pigeon flu virus, in an amount sufficient to produce an immunogenic response in a typical patient. Because viruses are composed of matter, the claim is directed to a statutory category, *e.g*., a composition of matter (*Step 1: YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The recited live attenuated virus is a nature-based product that must be compared to its naturally occurring counterpart to determine if it has markedly different characteristics than the counterpart. Here, the closest natural counterpart is the naturally occurring Pigeon flu virus from which the live attenuated virus was mutated. When the live attenuated virus is compared to this counterpart, the comparison indicates that the live attenuated virus has a different structural characteristic (the nucleotide sequence of its polymerase gene was changed due to the mutation), which has resulted in the live attenuated virus having a different functional characteristic (reduced virulence). No mutations of this gene are known to occur in nature. Thus, under the holding in Myriad, this structural difference is a markedly different characteristic, because it causes the claimed virus to have a nucleotide sequence that is different from anything found in nature. Association for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2119 (2013). While in other fact patterns, a functional change may be enough by itself to confer eligibility, for this claim the functional change is a result of the structural change and thus is inseparable from it. Because the live attenuated virus has markedly different characteristics from what exists in nature, it is not a "product of nature" exception. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Note that because the analysis of this claim ends at Step 2A, the Step 2B analysis is not performed. Thus, the examiner would not need to evaluate the significantly more considerations for this claim.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

Claim 2: Eligible.

The claim recites a vaccine comprising inactivated Pigeon flu virus. Based on the plain meaning of "vaccine", and the specification's definition of "inactivated Pigeon flu virus", the broadest reasonable interpretation of the claim is dead Pigeon flu virus that has been structurally altered by contacting it with formalin so that its nucleic acids are chemically modified in a manner that does not occur in nature and it can no longer reproduce, in an amount sufficient to produce an immunogenic response in a typical patient. Because viruses are composed of matter, the claim is directed to a statutory category, *e.g.*, a composition of matter (*Step 1: YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The recited inactivated virus is a nature-based product that must be compared to its naturally occurring counterpart to determine if it has markedly different characteristics than the counterpart. Here, the closest natural counterpart is the naturally occurring Pigeon flu virus. When the inactivated virus is compared to this counterpart, the comparison indicates that the inactivated virus has a different structural characteristic (its exposure to formalin has chemically modified its nucleic acids in a manner that does not occur in nature), which has resulted in the inactivated virus having different functional characteristics (inability to replicate or cause disease). Like the Chakrabarty bacterium, which had markedly different characteristics "due to the additional plasmids and resultant 'capacity for degrading oil,'" Myriad, 133 S. Ct. at 2117, the inactivated virus has markedly different characteristics, due to the non-natural chemical modification of its nucleic acids and the resultant change in the virus's ability to replicate or cause disease. While in other fact patterns, a functional change may be enough by itself to confer eligibility, for this claim the functional change is a result of the structural change and thus is inseparable from it. Because the inactivated virus has markedly different characteristics from what exists in nature, it is not a "product of nature" exception. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Note that because the analysis of this claim ends at Step 2A, the Step 2B analysis is not performed. Thus, the examiner would not need to evaluate the significantly more considerations for this claim. If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

Claim 3: Ineligible.

The claim recites a vaccine comprising Peptide F and a pharmaceutically acceptable carrier. Based on the plain meaning of "vaccine" and "pharmaceutically acceptable carrier", the broadest reasonable interpretation (BRI) of the claim is a sufficient amount of Peptide F to produce an immunogenic response in a typical patient, which is mixed with a pharmaceutically sufficient amount of a carrier such as water. Thus, one embodiment within the BRI is a mixture of Peptide F and water. Because the peptide and carrier are composed of matter, the claim is directed to a statutory category, *e.g.*, a composition of matter (*Step 1: YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The recited mixture of Peptide F and water is a nature-based product that must be compared to its closest naturally occurring counterpart to determine if it has markedly different characteristics than the counterpart. Because Peptide F and water do not occur together in nature, there is no naturally occurring counterpart mixture for comparison, and so the claimed mixture is compared to its naturally occurring components, *i.e.*, Peptide F, and water. Peptide F is naturally occurring, and water

is naturally occurring, so neither would be eligible as claimed on their own. While the mixture of these two naturally occurring components is novel and does not occur in nature, there is no indication that mixing these components changes the structure, function, or other properties of the peptide or water. For example, the claim encompasses a mixture where the peptide is heterogeneously dispersed in the water, but such heterogeneous mixing does not change the structure, function, or other properties of the peptide or the water in any marked way. Instead, the peptide retains its naturally occurring structure and function, and is merely dispersed in the water, which also retains its naturally occurring structure and function. Thus, for at least one embodiment within the broadest reasonable interpretation, the claimed mixture as a whole does not display markedly different characteristics compared to the naturally occurring counterparts. Accordingly, each component (the peptide and the carrier) is a "product of nature" exception, and the claim is directed to at least one exception (*Step 2A: YES*).

Next, the claim as a whole is analyzed to determine whether any additional element, or combination of elements, is sufficient to ensure that the claim amounts to significantly more than the exceptions. Because the component elements (the peptide and carrier "product of nature" exceptions) do not occur together in nature and are not markedly changed by their combination into a mixture, each is considered as an additional element to the other. This consideration provides an opportunity to explore whether this combination of "products of nature" amounts to significantly more than the products themselves. As discussed above, mixing the peptide with a carrier such as water does not markedly change the characteristics of either component, because each component continues to have the same properties in the mixture as it had alone. In addition, using a carrier in a peptide vaccine was well-understood, routine & conventional prior to applicant's invention and at the time of filing the application, so the mixing of the peptide and carrier, when recited at this high level of generality, does not meaningfully limit the claim. Thus, the claim as a whole does not amount to significantly more than each "product of nature" by itself (*Step 2B: NO*). The claim does not qualify as eligible subject matter.

A rejection of claim 3 should identify the exceptions by pointing to the nature-based products in the claim (the peptide and carrier) and explaining why they lack markedly different characteristics from their naturally occurring counterparts, *e.g.*, because there are no changes in structure, function, or other characteristics. The rejection should also explain that combining the peptide and carrier does not amount to significantly more than the exceptions, because their combination is well-understood, routine and conventional in the field.

If the examiner believes that it would be helpful to cite an analogous court decision, the rejection could include an explanation of how the claimed mixture is like the novel bacterial mixture of Funk Brothers, which was held ineligible because each species of bacteria in the mixture (like each component in the peptide-carrier mixture) continued to have "the same effect it always had", *i.e.*, it lacked markedly different characteristics. Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131 (1948), discussed in Myriad Genetics, 133 S. Ct. at 2117 (explaining that the bacterial mixture of Funk Brothers "was not patent eligible because the patent holder did not alter the bacteria in any way").

Claim 4: Eligible.

The claim recites a vaccine comprising Peptide F in a pharmaceutically acceptable carrier selected from the group consisting of a cream, emulsion, gel, liposome, nanoparticle, or ointment. Based on the plain meaning of "vaccine" and "pharmaceutically acceptable carrier", the broadest reasonable interpretation (BRI) of the claim is a sufficient amount of Peptide F to produce an immunogenic response in a typical patient, which is mixed with a sufficient amount of other substances to produce a carrier form suitable for administration to a patient. The BRI thus encompasses, for example, a

vaccine comprising Peptide F in a carrier that is a cream. Because the plain meaning of a "cream" in the pharmaceutical arts is a semi-solid homogeneous emulsion comprising water and oil, the recitation of a cream necessarily requires (i) the presence of water and an oil (such as naturally occurring cottonseed oil) in addition to Peptide F, and (ii) that the water and oil be structurally arranged into a homogenous emulsion to produce a semi-solid form. Thus, one embodiment within the BRI is an emulsion comprising Peptide F mixed with small uniform droplets of cottonseed oil that are homogenously dispersed in water. Because the peptide and the carrier are composed of matter, the claim is directed to a statutory category, *e.g*., a composition of matter (*Step 1: YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The claimed cream containing Peptide F, cottonseed oil, and water is a nature-based product that must be compared to its closest naturally occurring counterpart to determine if it has markedly different characteristics than the counterpart. Here, all three substances (the peptide, cottonseed oil, and water) do not occur together in nature, so there is no naturally occurring counterpart mixture for comparison. The mixture is therefore compared to its naturally occurring components, *i.e.*, Peptide F, cottonseed oil, and water. The claimed cream has different structural and physical characteristics than its naturally occurring components, for example the oil droplets are small, uniform in size, and homogenously dispersed in the water, which causes the resultant cream to have a semi-solid and non-flowable form at room temperature as compared to the oil and water, which are both flowable liquids at room temperature in nature. Because the oil and water are emulsified, the cream will also adhere to a patient's skin or mucous membranes much longer than oil or water in their natural non-emulsified form, thus permitting a sufficient amount of peptide to transfer from the cream into the patient's tissues where it will then stimulate an immune response. In contrast, the oil or water, if used in their natural state, would simply slide off the patient's skin after a short time. The cream's changed form and adherence are marked differences in structural and physical characteristics as compared to the natural counterparts, and therefore the cream is not a "product of nature" exception. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Note that because the analysis of this claim ends at Step 2A, the Step 2B analysis is not performed. Thus, the examiner would not need to evaluate the significantly more considerations for this claim. If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

Practice Note: The BRI of claim 4 also encompasses cream embodiments in which the oil is a non-naturally occurring oil, or is a naturally occurring oil other than cottonseed oil, or in which the homogenous emulsion is a water-in-oil emulsion instead of an oil-in-water emulsion, as well as embodiments in which the carrier is something other than a cream, *e.g*., a liposome or nanoparticle carrier. If the examiner were to analyze such embodiments for markedly different characteristics, the analysis may differ slightly due to the choice of different counterparts, but the same result of eligibility would be achieved because in every embodiment, the plain meaning of each carrier recited in the claim requires that the carrier have structural and physical characteristics that distinguish it from the closest counterpart in nature.

Claim 5: Eligible.

The claim recites a vaccine comprising Peptide F and an immuno-effective amount of an aluminum salt adjuvant. Based on the plain meaning of "vaccine" and "immuno-effective amount", the broadest reasonable interpretation (BRI) of the claim is a mixture of (i) a sufficient amount of Peptide F to produce an immunogenic response in a typical patient, and (ii) a sufficient amount of an aluminum salt adjuvant (*e.g*., aluminum phosphate; $AlPO_4$) to increase the vaccine's immunogenicity (measured here by seroprotection rate) to a level high enough to effectively vaccinate a typical patient. Thus,

one embodiment within the BRI is a mixture of Peptide F with a sufficient amount of aluminum phosphate to increase the vaccine's immunogenicity. Because the peptide and adjuvant are composed of matter, the claim is directed to a statutory category, *e.g*., a composition of matter (*Step 1: YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The claimed mixture of Peptide F and aluminum phosphate is a nature-based product that must be compared to its closest naturally occurring counterpart to determine if it has markedly different characteristics than the counterpart. Because Peptide F and aluminum phosphate do not occur together in nature, there is no naturally occurring counterpart mixture for comparison, and so the claimed mixture is compared to its naturally occurring components, *i.e.*, Peptide F, and the adjuvant (*e.g.*, aluminum phosphate). There is no indication that mixing these components changes the structure of the peptide or aluminum phosphate. However, the mixture has a changed functional property, in that the immunogenicity of the mixture is different (higher) than the mere "sum" of the immunogenicity of the individual components. In other words, the peptide by itself has poor immunogenicity (30% seroprotection rate) and the adjuvant by itself has no immunogenicity (0% seroprotection rate) with respect to Pigeon flu virus, but when combined, the resultant mixture has a greatly enhanced immunogenicity (80% seroprotection rate) with respect to Pigeon flu virus. The mixture's changed immunogenicity is a marked difference in functional characteristics as compared to the natural counterparts, and therefore the mixture is not a "product of nature" exception. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Note that because the analysis of this claim ends at Step 2A, the Step 2B analysis is not performed. Thus, the examiner would not need to evaluate the significantly more considerations for this claim. If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

Practice Note: The BRI of claim 5 also encompasses embodiments in which the adjuvant is a non-naturally occurring aluminum salt, or is a naturally occurring aluminum salt other than aluminum phosphate. If the examiner were to analyze such an embodiment for markedly different characteristics, the analysis may differ slightly due to the choice of different counterparts, but the same result of eligibility would be achieved because in every embodiment, the immuno-effective amount of the adjuvant will result in the claimed mixture exhibiting the same marked difference in immunogenicity described in the preceding analysis.

Claim 6: Eligible.

The claim recites a vaccine comprising Peptide F, an immuno-effective amount of an aluminum salt adjuvant, and a pharmaceutically acceptable carrier. Based on the plain meaning of "vaccine", "immuno-effective amount", and "pharmaceutically acceptable carrier", the broadest reasonable interpretation of the claim is a mixture of (i) a sufficient amount of Peptide F to produce an immunogenic response in a typical patient, (ii) a sufficient amount of an aluminum salt adjuvant (*e.g*., aluminum phosphate; $AlPO_4$) to increase the vaccine's immunogenicity (measured here by seroprotection rate) to a level high enough to effectively vaccinate a typical patient, and (iii) a pharmaceutically sufficient amount of a carrier such as water. Thus, one embodiment within the BRI is a mixture of Peptide F, a sufficient amount of aluminum phosphate to increase the vaccine's immunogenicity, and water. Because the peptide, adjuvant, and carrier are composed of matter, the claim is directed to a statutory category, *e.g*., a composition of matter (*Step 1: YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The claimed mixture of Peptide F, aluminum phosphate, and water is a nature-based product that must be

compared to its closest naturally occurring counterpart to determine if it has markedly different characteristics than the counterpart. Here, all three substances (the peptide, aluminum phosphate, and water) do not occur together in nature, so there is no naturally occurring counterpart mixture for comparison. However, aluminum phosphate does occur naturally in combination with water (*e.g.*, in soil). Accordingly, the closest naturally occurring counterparts to which the claimed mixture is compared are Peptide F, and the naturally occurring water/aluminum phosphate combination. There is no indication that mixing the peptide with the water/aluminum phosphate combination changes the structure of either component, but the mixture does have a changed functional property, in that the immunogenicity of the mixture is different (higher) than the mere "sum" of the immunogenicity of the individual components. In other words, the peptide by itself has poor immunogenicity (30% seroprotection rate), and the water/aluminum phosphate combination by itself has no immunogenicity (0% seroprotection rate) with respect to Pigeon flu virus, but when combined, the resultant mixture has a greatly enhanced immunogenicity (80% seroprotection rate) with respect to Pigeon flu virus. The mixture's changed immunogenicity is a marked difference in functional characteristics as compared to the natural counterparts, and therefore the mixture is not a "product of nature" exception. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Note that because the analysis of this claim ends at Step 2A, the Step 2B analysis is not performed. Thus, the examiner would not need to evaluate the significantly more considerations for this claim. If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

Practice Note: The BRI of claim 6 also encompasses embodiments in which the adjuvant is a non-naturally occurring aluminum salt, or is a naturally occurring aluminum salt other than aluminum phosphate, and embodiments in which the carrier is something other than water. If the examiner were to analyze such an embodiment for markedly different characteristics, the analysis may differ slightly due to the choice of different counterparts, but the same result of eligibility would be achieved because in every embodiment, the immuno-effective amount of the adjuvant will result in the claimed mixture exhibiting the same marked difference in immunogenicity described in the preceding analysis.

Claim 7: Eligible.

The claim recites a vaccine delivery device comprising a microneedle array that is coated with a vaccine comprising Peptide F. Based on the plain meaning of "microneedle array" and "vaccine", the broadest reasonable interpretation (BRI) of the claim is an array of small solid needles coated with a sufficient amount of Peptide F to produce an immunogenic response in a typical patient. Thus, one embodiment within the BRI is an array of small solid needles (the microneedle array) coated with Peptide F. The microneedle array is a manufacture and the peptide is composed of matter; thus, the claim is directed to at least one statutory category, *e.g.*, a manufacture and/or a composition of matter (*Step 1: YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The microneedle array is not a nature-based product, but the Peptide F is a nature-based product that must be compared to its closest naturally occurring counterpart (naturally occurring Peptide F) to determine if it has markedly different characteristics than the counterpart in its natural state as part of the virus. There is no indication in the specification that isolation changes any structural or functional characteristics of Peptide F, or that coating the needles in the array with Peptide F results in the peptide having any characteristics (structural, functional, or otherwise) that are different from the naturally occurring peptide in its natural state. Thus, the claimed peptide does not display

markedly different characteristics compared to the naturally occurring counterpart. Accordingly, the peptide is a "product of nature" exception, and the claim is directed to at least one exception (*Step 2A: YES*).

Next, the claim as a whole is analyzed to determine whether any additional element, or combination of elements, is sufficient to ensure that the claim amounts to significantly more than the exception. Besides the exception, the claim recites an additional element of the microneedle array, which is coated with the peptide. Prior to applicant's invention, and at the time the application was filed, coated microneedle arrays were known to most scientists in the field, but were not routinely or conventionally used to administer vaccines. The conventional delivery device was a syringe that was routinely pre-filled with the vaccine. Thus, the claim's recitation of a microneedle array coated with the peptide is an application of the exception with a particular manufacture that is not a conventional delivery device, and thus is more than a mere instruction to "apply" the peptide (the exception) using a well-understood, routine or conventional device in the field. It is an unconventional limitation that confines the exception to a particular useful application of the exception. Thus, the recitation of the coated microneedle array yields a claim as a whole that amounts to significantly more than the "product of nature" exception itself (*Step 2B: YES*). The claim is eligible.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance indicating that the peptide is a "product of nature" exception because it lacks markedly different characteristics from its naturally occurring counterpart, *e.g.*, because there are no changes in structure, function, or other characteristics. However, the claim is eligible because it recites a particular, unconventional limitation (the coated microneedle array) that confines the exception to a particular useful application, and that is more than a mere instruction to "apply" the exception using a well-understood, routine or conventional device in the field.

29. Diagnosing and Treating Julitis

This hypothetical example illustrates the application of the significantly more analysis to diagnostic and treatment claims using a hypothetical disease. Claims 1 and 7 are eligible in Step 2A, because they are not directed to any judicial exception. Claim 2 is ineligible, because it is directed to a judicial exception that could be termed either a law of nature or an abstract idea, and the recited additional elements do not amount to significantly more than the exception. Claims 3-6 are directed to the same exception, but are eligible in Step 2B because they recite specific and unconventional reagents and/or treatments that amount to significantly more than the exception.

Background

"Julitis" is an autoimmune disease affecting more than 17 million people in North America, which develops when the immune system mistakes normal skin cells for pathogens. Julitis causes chronic inflammation of the skin that results in an itchy and extremely painful rash on the face, hands, and feet. Conventionally, julitis is diagnosed by a physical examination of the characteristic rash. However, because the rash caused by julitis looks similar to rashes caused by rosacea, doctors often misdiagnosed people as having rosacea when they actually had julitis.

Applicant has discovered that the presence of a protein known as "JUL-1" in a person's body is indicative that the person has julitis. All julitis patients have JUL-1 in their plasma, skin, hair and nails, but this protein is not found in persons who do not have julitis (*e.g.*, patients with rosacea). Applicant discloses detecting JUL-1 by routine and conventional methods such as (i) physical biopsies of skin, hair or nails, or (ii) immunoassays in which a sample from a patient (*e.g.*, a plasma or skin sample) is contacted with an antibody to the protein being detected, and then binding between the antibody and the protein is detected using a laboratory technique such as fluoroscopy. In particular, applicant

discloses detecting JUL-1 using anti-JUL-1 antibodies that may be naturally occurring (*e.g.*, a human anti-JUL-1 antibody isolated from a patient known to have julitis), or non-naturally occurring (*e.g.*, a porcine anti-JUL-1 antibody created by injecting pigs with JUL-1, or a specific monoclonal antibody named "mAb-D33" that was created by applicant). Prior to applicant's invention, and at the time the application was filed, the use of porcine antibodies in veterinary therapeutics was known to most scientists in the field, but these antibodies were not routinely or conventionally used to detect human proteins such as JUL-1.

Prior to applicant's invention, and at the time the application was filed, julitis was conventionally treated with anti-tumor necrosis factor (TNF) antibodies, but for unknown reasons, some patients do not respond well to this conventional treatment. Because rosacea treatments (*e.g.*, antibiotics) are not effective against julitis, julitis patients who were misdiagnosed as having rosacea also did not respond well to the treatments they were given. Some anti-TNF antibodies are naturally occurring in patients with other autoimmune diseases such as lupus. Applicant has successfully treated julitis patients (even those who are non-responsive to anti-TNF antibodies) with topical vitamin D. Prior to applicant's invention, and at the time the application was filed, vitamin D was commonly used as an oral supplement to maintain bone health (*e.g.*, in fortified dairy products), but doctors were not commonly or routinely administering topical vitamin D to patients with julitis or other diseases.

Claims

1. A method of detecting JUL-1 in a patient, said method comprising:
   a. obtaining a plasma sample from a human patient; and
   b. detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with an anti-JUL-1 antibody and detecting binding between JUL-1 and the antibody.

2. A method of diagnosing julitis in a patient, said method comprising:
   a. obtaining a plasma sample from a human patient;
   b. detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with an anti-JUL-1 antibody and detecting binding between JUL-1 and the antibody; and
   c. diagnosing the patient with julitis when the presence of JUL-1 in the plasma sample is detected.

3. A method of diagnosing julitis in a patient, said method comprising:
   a. obtaining a plasma sample from a human patient;
   b. detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with a porcine anti-JUL-1 antibody and detecting binding between JUL-1 and the porcine antibody; and
   c. diagnosing the patient with julitis when the presence of JUL-1 in the plasma sample is detected.

4. A method of diagnosing julitis in a patient, said method comprising:
   a. obtaining a plasma sample from a human patient;
   b. detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with antibody mAb-D33 and detecting binding between JUL-1 and antibody mAb-D33; and
   c. diagnosing the patient with julitis when the presence of JUL-1 in the plasma sample is detected.

5. A method of diagnosing and treating julitis in a patient, said method comprising:
   a. obtaining a plasma sample from a human patient;

b. detecting whether JUL-1 is present in the plasma sample;
c. diagnosing the patient with julitis when the presence of JUL-1 in the plasma sample is detected; and
d. administering an effective amount of topical vitamin D to the diagnosed patient.

6. A method of diagnosing and treating julitis in a patient, said method comprising:
   a. obtaining a plasma sample from a human patient;
   b. detecting whether JUL-1 is present in the plasma sample;
   c. diagnosing the patient with julitis when the presence of JUL-1 in the plasma sample is detected; and
   d. administering an effective amount of anti-tumor necrosis factor (TNF) antibodies to the diagnosed patient.

7. A method of treating a patient with julitis, the method comprising administering an effective amount of anti-TNF antibodies to a patient suffering from julitis.

Analysis

Claim 1: Eligible.

The claim recites a series of steps or acts, including detecting the presence of JUL-1 in a plasma sample. Thus, the claim is directed to a process, which is one of the statutory categories of invention (*Step 1: YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The claim recites steps of obtaining a plasma sample from a patient (step a) and detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with an anti-JUL-1 antibody and detecting resultant binding between JUL-1 and the antibody (step b). These steps do not recite or describe any recognized exception. *See, e.g.*, Mayo Collaborative Svcs. v. Prometheus Labs., 566 U.S. __, 132 S. Ct. 1289, 1297 (2012) (recited steps of administering a drug to a patient and determining the resultant level of 6-thioguanine in the patient "are not themselves natural laws"). Accordingly, the claim is not directed to an exception (*Step 2A: NO*), and is eligible.

Note that although nature-based product limitations are recited in the claim (*e.g.*, the plasma sample and JUL-1), analysis of the claim as a whole indicates that the claim is focused on a process of detecting whether JUL-1 is present in a plasma sample, and is not focused on the products *per se*. Thus, there is no need to perform the markedly different characteristics analysis on the recited nature-based product limitations. In addition, note that because the analysis of this claim ends with eligibility at Step 2A, the Step 2B analysis does not need to be performed. Thus, the examiner would not need to evaluate the significantly more considerations for this claim.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

Claim 2: Ineligible.

The claim recites a series of steps or acts, including detecting the presence of JUL-1 in a plasma sample. Thus, the claim is directed to a process, which is one of the statutory categories of invention (*Step 1: YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. In step c, the claim recites diagnosing the patient with julitis when the presence of JUL-1 in the plasma sample is detected, which describes a correlation or relationship between the presence of JUL-1 in a patient's

plasma and the presence of julitis in the patient. This limitation sets forth a judicial exception, because this type of correlation is a consequence of natural processes, similar to the naturally occurring correlation found to be a law of nature by the Supreme Court in Mayo). Additionally, step c could be performed by a human using mental steps or basic critical thinking, which are types of activities that have been found by the courts to represent abstract ideas (*e.g.*, the mental comparison in Ambry Genetics, or the diagnosing an abnormal condition by performing clinical tests and thinking about the results in Grams). Thus, the claim is directed to at least one exception (*Step 2A: YES*), which may be termed a law of nature, an abstract idea, or both. Note that although the claim recites several nature-based product limitations (*e.g.*, the plasma sample and JUL-1), the claim as a whole is focused on a process of detecting whether JUL-1 is present in a plasma sample, and is not focused on the products *per se*. Thus, there is no need to perform the markedly different characteristics analysis on the recited nature-based product limitations.

Next, the claim as a whole is analyzed to determine whether any element, or combination of elements, is sufficient to ensure that the claim amounts to significantly more than the exception. Besides the law of nature, the claim recites additional steps of obtaining a plasma sample from a human patient (step a), and detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with an anti-JUL-1 antibody and detecting resultant binding between JUL-1 and the antibody (step b). Obtaining a sample in order to perform tests is well-understood, routine and conventional activity for those in the field of diagnostics. Further, the step is recited at a high level of generality such that it amounts to insignificant presolution activity, *e.g.*, a mere data gathering step necessary to use the correlation. Detecting whether JUL-1 is present in the plasma sample merely instructs a scientist to use any detection technique with any generic anti-JUL-1 antibody. When recited at this high level of generality, there is no meaningful limitation, such as a particular or unconventional machine or a transformation of a particular article, in this step that distinguishes it from well-understood, routine, and conventional data gathering activity engaged in by scientists prior to applicant's invention, and at the time the application was filed, *e.g.*, the routine and conventional techniques of detecting a protein using an antibody to that protein. Further, it is well established that the mere physical or tangible nature of additional elements such as the obtaining and detecting steps does not automatically confer eligibility on a claim directed to an abstract idea (*see*, *e.g.*, Alice Corp. v. CLS Bank Int'l, 134 S.Ct. 2347, 2358-59 (2014)).

Consideration of the additional elements as a combination also adds no other meaningful limitations to the exception not already present when the elements are considered separately. Unlike the eligible claim in Diehr in which the elements limiting the exception are individually conventional, but taken together act in concert to improve a technical field, the claim here does not invoke any of the considerations that courts have identified as providing significantly more than an exception. Even when viewed as a combination, the additional elements fail to transform the exception into a patent-eligible application of that exception. Thus, the claim as a whole does not amount to significantly more than the exception itself *(Step 2B: NO).* The claim is not eligible.

A rejection of claim 2 should identify step c as an exception by pointing to it in the claim and explaining why it is an exception, *e.g.*, that the recited correlation is a law of nature because it is a consequence of a natural process in the body, and/or that the critical thinking step is an abstract idea similar to those found by the courts to be an exception. The rejection should also identify the additional elements in the claim and explain why they do not amount to significantly more, in this case, because they merely add data gathering and well-understood, routine and conventional activities that do not impose meaningful limits on the law of nature.

Claim 3: Eligible.

The claim recites a series of steps or acts, including detecting the presence of JUL-1 in a plasma sample. Thus, the claim is directed to a process, which is one of the statutory categories of invention (*Step 1: YES*). Because claim 3 recites the same correlation and critical thinking step (step c) as claim 2, which as explained above is a law of nature and/or an abstract idea, the claim is directed to a judicial exception (*Step 2A: YES*). Although this claim recites several nature-based product limitations (the plasma sample, JUL-1, and the antibody), there is no need to perform the markedly different characteristics analysis on them, for the reasons discussed above for claim 2.

Next, the claim as a whole is analyzed to determine whether any element, or combination of elements, is sufficient to ensure that the claim amounts to significantly more than the exception. Besides the exception, the claim recites additional steps of obtaining a plasma sample from a human patient (step a), and detecting whether JUL-1 is present in the plasma sample by contacting the plasma sample with a porcine anti-JUL-1 antibody and detecting resultant binding between JUL-1 and the antibody (step b). The additional element of obtaining a plasma sample (step a) does not by itself add significantly more, for the reasons discussed above for claim 2. Step b, however, also requires detecting using a porcine anti-JUL-1 antibody. Prior to applicant's invention, and at the time the application was filed, the use of porcine antibodies in veterinary therapeutics was known to most scientists in the field. But significantly, there is no evidence that porcine antibodies were routinely or conventionally used to detect human proteins such as JUL-1. Thus, the claim's recitation of detecting JUL-1 using a porcine antibody is an unconventional step that is more than a mere instruction to "apply" the correlation and critical thinking step (the exception) using well-understood, routine or conventional techniques in the field. Whether taken alone or as a combination with the other additional elements, the recitation of detecting JUL-1 using a porcine anti-JUL-1 antibody yields a claim as a whole that amounts to significantly more than the exception itself (*Step 2B: YES*). The claim is eligible.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance indicating that the correlation and critical thinking step (step c) is a law of nature and/or an abstract idea. However, the claim is eligible because it recites additional limitations that when considered as a combination are unconventional steps that are more than a mere instruction to "apply" the exception using well-understood, routine or conventional techniques in the field.

Claim 4: Eligible.

The claim recites a series of steps or acts, including detecting the presence of JUL-1 in a plasma sample. Thus, the claim is directed to a process, which is one of the statutory categories of invention (*Step 1: YES*). Because claim 4 recites the same correlation and critical thinking step (step c) as claim 2, which as explained above is a law of nature and/or an abstract idea, the claim is directed to a judicial exception (*Step 2A: YES*). Although this claim recites several nature-based product limitations (the plasma sample, JUL-1, and the antibody), there is no need to perform the markedly different characteristics analysis on them, for the reasons discussed above for claim 2.

Next, the claim as a whole is analyzed to determine whether any element, or combination of elements, is sufficient to ensure that the claim amounts to significantly more than the exception. Besides the exception, the claim recites the additional elements of obtaining a plasma sample from a human patient (step a) and detecting the presence of JUL-1 in the sample by contacting the plasma sample with antibody mAb-D33 and detecting resultant binding between the antibody and JUL-1 (step b). The additional element of obtaining a plasma sample (step a) does not add significantly more by itself, for the reasons discussed above for claim 2. Step b, however, requires detecting using a specific anti-

JUL-1 antibody (mAb-D33). Prior to applicant's invention, and at the time the application was filed, antibody mAb-D33 was not routinely or conventionally used to detect human proteins such as JUL-1. Thus, the claim's recitation of detecting JUL-1 using mAb-D33 is an unconventional step that is more than a mere instruction to "apply" the correlation and critical thinking step (the exception) using well-understood, routine or conventional techniques in the field. Whether taken alone or as a combination with the other additional elements, the recitation of detecting JUL-1 using mAb-D33 yields a claim as a whole that amounts to significantly more than the exception itself (*Step 2B: YES*). The claim is eligible.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance indicating that the correlation and critical thinking step (step c) is a law of nature and/or an abstract idea. However, the claim is eligible because it recites additional limitations that when considered as a combination are unconventional steps that are more than a mere instruction to "apply" the exception using well-understood, routine or conventional techniques in the field.

Claim 5: Eligible.

The claim recites a series of steps or acts, including detecting the presence of JUL-1 in a plasma sample. Thus, the claim is directed to a process, which is one of the statutory categories of invention (*Step 1: YES*). Because claim 5 recites the same correlation and critical thinking step (step c) as claim 2, which as explained above is a law of nature and/or an abstract idea, the claim is directed to a judicial exception (*Step 2A: YES*). Although the claim recites several nature-based product limitations (the plasma sample, JUL-1, and vitamin D), there is no need to perform the markedly different characteristics analysis on them, for the reasons discussed above for claim 2.

Next, the claim as a whole is analyzed to determine whether any element, or combination of elements, is sufficient to ensure that the claim amounts to significantly more than the exception. Besides the exception, the claim recites the additional elements of obtaining a plasma sample from a human patient (step a) and detecting the presence of JUL-1 in the sample (step b). When considered individually, steps a and b by themselves do not add significantly more to the exception for the reasons discussed above for claim 2 (*e.g.,* step b in this claim is recited at an even higher level of generality than in claim 2, that encompasses any protein detection method, whether or not it uses antibodies). However, this claim further recites an additional element of administering an effective amount of topical vitamin D to the diagnosed patient (step d). Vitamin D was known to doctors, and was routinely and conventionally used as an oral supplement to maintain bone health prior to applicant's invention, and at the time the application was filed. However, mere knowledge of vitamin D or its use in other ways to treat other medical conditions does not make the administration of topical vitamin D to treat julitis a conventional step that those in this field would routinely practice. The evaluation turns on whether the use of topical vitamin D was widely prevalent in the field at the time the invention was made and the application was filed. Because it was not, the recitation of administering topical vitamin D is an unconventional step that is more than a mere instruction to "apply" the correlation and critical thinking step (the exception) using well-understood, routine or conventional techniques in the field. Whether taken alone or as a combination with the other additional elements, the recitation of administering topical vitamin D yields a claim as a whole that amounts to significantly more than the exception itself (*Step 2B: YES*). The claim is thus eligible.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance indicating that the correlation and critical thinking step (step c) is a law of nature and/or an abstract idea. However, the claim is eligible because it recites additional limitations that when considered as a combination are unconventional steps that are more

than a mere instruction to "apply" the exception using well-understood, routine or conventional techniques in the field.

Claim 6: Eligible.

The claim recites a series of steps or acts, including detecting the presence of JUL-1 in a plasma sample. Thus, the claim is directed to a process, which is one of the statutory categories of invention (*Step 1: YES*). Because claim 6 recites the same correlation and critical thinking step (step c) as claim 2, which as explained above is a law of nature and/or an abstract idea, the claim is directed to a judicial exception (*Step 2A: YES*). Although the claim recites several nature-based product limitations (the plasma sample, JUL-1, and the anti-TNF antibodies), there is no need to perform the markedly different characteristics analysis on them, for the reasons discussed above for claim 2.

Next, the claim as a whole is analyzed to determine whether any element, or combination of elements, is sufficient to ensure that the claim amounts to significantly more than the exception. Besides the exception, the claim recites the same additional elements of obtaining a plasma sample from a human patient (step a) and detecting the presence of JUL-1 in the sample (step b) as claim 5. When considered individually, steps a and b do not by themselves add significantly more to the exception for the reasons discussed above for claims 2 and 5. This claim further recites an additional element of administering an effective amount of anti-TNF antibodies to the diagnosed patient (step d). Prior to applicant's invention, and at the time the application was filed, however, administering these antibodies to treat a patient diagnosed with julitis was well-understood, routine and conventional activity engaged in by doctors in the field. Further, it is well established that the mere physical or tangible nature of additional elements such as the obtaining, detecting, and administering steps does not automatically confer eligibility on a claim directed to an exception (*see*, *e.g.*, Alice Corp., 134 S.Ct. at 2358-59).

When the additional elements are viewed as a combination, however, the additional elements (steps a, b and d) amount to a claim as a whole that adds meaningful limits on the use of the exception (the correlation and critical thinking step). The totality of these steps including the recitation of a particular treatment (administration of an effective amount of anti-TNF antibodies) in step d integrate the exception into the diagnostic and treatment process, and amount to more than merely diagnosing a patient with julitis and instructing a doctor to generically "treat it." Further, the combination of steps, which is not routine and conventional, ensures that patients who have julitis will be accurately diagnosed (due to the detection of JUL-1 in their plasma) and properly treated with anti-TNF antibodies, as opposed to being misdiagnosed as having rosacea as was previously commonplace. *See* Diamond v. Diehr, 450 U.S. 175, 188 (1981) ("a new combination of steps in a process may be patentable even though all the constituents of the combination were well known and in common use before the combination was made"). Thus, the administration of anti-TNF antibodies, when considered as a combination with the other additional elements, yields a claim as a whole that amounts to significantly more than the exception itself (*Step 2B: YES*). The claim is eligible.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance indicating that the correlation and critical thinking step (step c) is a law of nature and/or an abstract idea. However, the claim is eligible because it recites additional limitations that when considered as a combination are a meaningful way of applying the exception that is more than a mere instruction to "apply" the exception.

Claim 7: Eligible.

The claim recites at least one step or act, *e.g.*, administering an effective amount of anti-TNF antibodies to a patient suffering from julitis. Thus, the claim is directed to a process, which is one of the statutory categories of invention (*Step 1: YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. Although the claim recites a nature-based product limitation (the anti-TNF antibodies), analysis of the claim as a whole indicates that the claim is focused on a process of practically applying the product to treat a particular disease (julitis), and not on the product *per se*. Accordingly, it is not necessary to perform the markedly different characteristics analysis on the antibodies. The recited step of administering antibodies to a patient suffering from julitis does not recite or describe any recognized exception. *See, e.g.*, Mayo, 132 S. Ct. at 1297 (recited steps of administering a drug to a patient and determining the resultant level of 6-thioguanine in the patient "are not themselves natural laws"). Thus, the claim is not directed to an exception (*Step 2A: NO*). The claim is eligible.

Note that because the analysis of this claim ends in eligibility at Step 2A, the Step 2B analysis does not need to be performed. Thus, the examiner would not need to evaluate the significantly more considerations for this claim.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

30. Dietary Sweeteners

This example illustrates the application of the markedly different characteristics and significantly more analyses to claims reciting hypothetical nature-based products including mixtures. It also illustrates the importance of applying the broadest reasonable interpretation in the eligibility analysis, and how that interpretation assists in the identification of appropriate naturally occurring counterparts of claimed nature-based products. Hypothetical claims 1 and 2 are ineligible, because the claimed nature-based products lack markedly different characteristics from what exists in nature, and the claims fail to amount to significantly more than the exceptions (even though claim 2 recites specific amounts of the components in the nature-based product). Hypothetical claims 3-6 are eligible in Step 2A, because the claimed nature-based products have markedly different characteristics from what exists in nature.

Background

The "Texas mint" plant is a relative of stevia, which has a thin liquid sap containing about 10% texiol (a newly discovered glycoside similar to rebaudioside A). When the Texas mint plant is damaged, *e.g.*, by a leaf or stem breaking, sap is released from the injury site, and over time dries to form irregular crystals of texiol. Texiol is lower in calories and tastes sweeter than table sugar, but it has a bitter aftertaste. Texiol can be used as crystals or as a powder, and is soluble in water at various concentrations. Applicant filed an application defining a "dietary sweetener" as one of the following formulations, noting that all percentages are by weight:

- A dietary sweetener comprising texiol mixed with other components such as water to form a heterogeneous or homogenous mixture, *e.g.*, a solution or suspension. Applicant discloses that trained sensory panels reviewed formulations having varying concentrations of texiol in water, and found that the sensory perceptions of texiol's sweetness and bitter aftertaste both increased with concentration, *e.g.*, higher concentrations of texiol were perceived as having stronger sweet and bitter tastes. Based on the panel's review, and from a consumer's perspective, applicant discloses a preferred dietary sweetener comprising 1-5% texiol and at least 90% water. This preferred sweetener retains the naturally occurring texiol's sweetness and bitter aftertaste.
- A dietary sweetener comprising texiol mixed with water and Compound N (a natural flavor excreted from mushrooms and having a mild umami taste). Applicant discloses that when combined with texiol in particular amounts, Compound N neutralizes the bitter aftertaste of

texiol. Applicant discloses that this neutralization does not involve a chemical reaction. The same sensory panel tasted mixtures having various concentrations of Compound N and texiol, and found that a formulation comprising 1-5% texiol, 1-2% Compound N, and the balance water produced the most palatable results for a dietary sweetener with no bitter aftertaste. When Compound N is added in the specified amount, the changed taste perception occurs whether or not the texiol is fully dissolved, *e.g*., even when large crystals of texiol are used.

- A dietary sweetener solid gel formulation comprising 5% texiol mixed with water and/or fruit juice and sufficient pectin to provide a solid gel. The Texas mint plant does not contain pectin in nature. Solid gel formulations are useful commercial sweeteners because their solid, jelly-like consistency makes them spreadable onto other foods, such as bread, cake layers, or pastry dough. Solid gels can also be formed into candies such as jellybeans. Applicant discloses that the same sensory panel tasted the gel formulation and found that it had improved organoleptic properties (*e.g.*, a more pleasant mouthfeel) and a solid but easily-spreadable consistency as compared to naturally occurring texiol (either in the sap or crystallized).
- A dietary sweetener comprising texiol in granular form for use by consumers. Naturally occurring texiol forms irregular crystals that aggregate into large chunks of varying size and shape. Due to this variation, sweeteners formed from these irregular crystals do not have consistent and commercially acceptable dissolution rates. For example, a consumer attempting to sweeten iced tea with irregular texiol crystals will typically experience a need to add more than the expected amount of texiol in order to obtain the desired level of sweetness, because the larger particles of texiol dissolve more slowly (if at all) than the smaller particles even with vigorous stirring. The presence of these undissolved crystals may also cause an undesirable gritty mouth feel as the sweetened tea is consumed. To solve the problem of inconsistent and slow dissolution rates, applicant has produced granulated texiol formulations having even and regular particle size distributions, *e.g*., by grinding or milling coarse texiol crystals into an even and regular powder, or by crystallizing texiol in a controlled manner that forms regularly sized and shaped crystals. Granular texiol having a particle size of X10 of 80 microns and X90 of 300 microns is preferred, because this particle size distribution results in a greatly increased (and consistent) dissolution rate in water-based liquids as compared to naturally occurring texiol crystals. The terms "X10" and "X90" refer to the median diameter of the particles, as measured on a volume basis by a laser diffraction particle sizing system. For "X10", 10 percent of the particles have a diameter smaller than the specified size, and 90 percent of the particles have a larger diameter, and for "X90", 90 percent of the particles have a diameter smaller than the specified size, and 10 percent of the particles have a larger diameter.
- A dietary sweetener comprising texiol in a controlled release formulation. Applicant discloses that the same sensory panel, upon tasting naturally occurring texiol, reported perceiving an immediate burst of sweetness that rapidly dissipated. Applicant discloses formulations that achieve controlled release (*e.g.*, release of specific amounts of texiol from the formulation at specific time intervals, or over a prolonged period of time) by mixing the texiol with other substances such as polymers and/or changing the form of the texiol so that a controlled perception of sweetness is achieved. For example, in one such formulation, texiol particles are encapsulated in a polymer-emulsifier mixture that delays release of the texiol as compared to unencapsulated (*e.g*., naturally occurring) texiol particles. These controlled release formulations prolong enjoyment of a texiol-sweetened product such as chewing gum, by altering the time over which texiol's sweetness is perceived.

Claims

1. A dietary sweetener comprising:
   texiol; and
   water.

2. A dietary sweetener comprising:
   1-5 percent texiol; and
   at least 90 percent water.

3. A dietary sweetener comprising:
   1-5 percent texiol;
   at least 90 percent water; and
   1-2 percent Compound N.

4. A dietary sweetener comprising:
   5 percent texiol;
   water, fruit juice, or a combination of water and fruit juice; and
   sufficient amounts of pectin to provide a solid gel.

5. A dietary sweetener comprising:
   granular particles of texiol having a particle diameter of X10 of 80 microns and X90 of 300 microns.

6. A dietary sweetener comprising texiol in a controlled release formulation.

Analysis

Claim 1: Ineligible

The claim recites a dietary sweetener comprising texiol and water. Based on the specification's definition of "dietary sweetener", the broadest reasonable interpretation (BRI) of the claim is a mixture of texiol and water in any amount that will be understood as a sweetener to those of ordinary skill in the art. Thus, the BRI covers the naturally occurring sap of the Texas mint plant, which contains texiol and water. Because texiol and water are composed of matter, the claim is directed to a statutory category, *e.g.*, a composition of matter (*Step 1*: *YES*).

The claim is then analyzed in Step 2A to determine whether it is directed to any judicial exception. As noted above, the BRI of this claim encompasses the naturally occurring sap. Because the sap is naturally occurring, it cannot have markedly different characteristics from how it exists in nature, and therefore the claimed mixture of texiol and water (*i.e.*, the sap) is a "product of nature" exception. Association for Molecular Pathology v. Myriad Genetics, 133 S. Ct. 2107, 2116 (2013) (naturally occurring things are "products of nature" which cannot be patented). Thus, the claim is directed to at least one exception (*Step 2A: YES*).

Next, the claim as a whole is analyzed to determine whether any additional element, or combination of elements, is sufficient to ensure that the claim amounts to significantly more than the exception. In this case, the combination as claimed occurs in nature (as sap) so there are no additional elements to the claimed combination. The claim is to a "product of nature" exception with nothing that adds significantly more (*Step 2B: NO*). Claim 1 is not eligible.

A rejection of claim 1 should identify the exception(s) by pointing to the nature-based product in the claim (the combination of texiol-water) and explaining that it is a "product of nature" exception

because it is naturally occurring. The rejection should also explain that because the combination of the texiol and water is the exception, there are no additional elements in the claim that could amount to significantly more than the exception.

If the examiner believes that it would be helpful to cite an analogous court decision, the rejection could include an explanation of how the claimed mixture is like the cloned mammals of Roslin, which were held ineligible because, as claimed, the cloned mammals lacked markedly different characteristics from their naturally occurring counterparts. In re Roslin Institute (Edinburgh), 750 F.3d 1333, 1339 (2014).

Claim 2: Ineligible

The claim recites a dietary sweetener comprising 1-5 percent texiol and at least 90 percent water. Based on the specification's definition of "dietary sweetener", the broadest reasonable interpretation (BRI) of the claim is a mixture of texiol and water in the specified amounts. In this case, the BRI does not cover the naturally occurring sap of the Texas mint plant, which contains a different amount of texiol. Because texiol and water are composed of matter, the claim is directed to a statutory category, *e.g.*, a composition of matter (*Step 1*: *YES*).

The claim is then analyzed in Step 2A to determine whether it is directed to any judicial exception. The claimed mixture is a nature-based product that is compared to its closest naturally occurring counterpart, in order to determine if it has markedly different characteristics from this counterpart. As noted above, the BRI of this claim is limited to the recited percentages and thus does not encompass the naturally occurring sap of the Texas mint plant. Accordingly, the closest naturally occurring counterpart is not the sap, but the naturally occurring texiol-water mixture in the sap. By comparing the claimed mixture and its component parts to the naturally occurring texiol-water mixture in the sap, all potential changes in characteristics can be investigated.

Texiol is naturally occurring, and water is naturally occurring, so neither would be eligible as claimed on its own. Although the combination as claimed is novel and does not occur in nature, there is no indication that mixing them in the recited amounts (*i.e.*, 1-5 percent texiol and at least 90 percent water) changes the structure, function, or other properties of the texiol or water in any marked way. Instead, the texiol retains its naturally occurring structure and properties (*e.g.*, its sweetness and bitter aftertaste), and is merely located in water, which also retains its naturally occurring structure and properties (*e.g.*, its liquid form at room temperature). These characteristics are also the same as the naturally occurring texiol and water in the sap, which is also a sweet liquid at room temperature. Thus, the claimed mixture as a whole does not display markedly different characteristics compared to the closest naturally occurring counterpart. Accordingly, each component (the texiol and the water) is a "product of nature" exception, and the claim is directed to at least one exception (*Step 2A: YES*).

Next, the claim as a whole is analyzed to determine whether any additional element, or combination of elements, is sufficient to ensure that the claim amounts to significantly more than the exceptions. Because the component elements (the texiol and water "product of nature" exceptions) do not occur together in nature as claimed (*i.e.*, in the recited amounts) and are not markedly changed by their combination into a mixture, each component is considered as an additional element to the other to determine whether their combination results in significantly more than the products of nature. This consideration of the texiol as an additional element to the water, and vice-versa, provides an opportunity to explore whether this combination of "products of nature" amounts to significantly more than the products themselves. As discussed above, mixing the sweetener with water does not markedly change the characteristics of either component, because each component continues to have the same properties in the mixture as it had alone. Prior to applicant's invention and at the time of

filing the application, mixing a sweetener with water (or vice-versa) was well-understood, routine and conventional in the field, as evidenced by, *e.g.*, the ubiquity of simple syrup and stevia-based liquid sweeteners. The recitation of specific amounts of texiol and water does not affect this analysis, because it was also well-understood, routine and conventional at the time to mix specific amounts of sweeteners with water (or vice-versa) and to vary the amounts of the combination, *e.g.*, to achieve commercially acceptable sweetness levels and provide sweeteners for different purposes. Thus, the mixing of texiol and water, when recited at this high level of generality, does not meaningfully limit the claim, and the claim as a whole does not amount to significantly more than each "product of nature" by itself (*Step 2B: NO*). The claim does not qualify as eligible subject matter.

A rejection of claim 2 should identify the exceptions by pointing to the nature-based product limitations in the claim (texiol and water) and explaining why they lack markedly different characteristics from their naturally occurring counterparts, *e.g.*, because there are no marked changes in structure, function or other characteristics. The rejection also should explain that mixing texiol and water does not amount to significantly more than the exceptions, because mixtures of sweeteners and water are well-understood, routine and conventional in the field.

If the examiner believes that it would be helpful to cite an analogous court decision, the rejection could include an explanation of how the claimed mixture is like the novel bacterial mixture of Funk Brothers, which was held ineligible because each species of bacteria in the mixture (like each component in the texiol mixture) continued to have "the same effect it always had", *i.e.*, it lacked markedly different characteristics. Funk Brothers Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 131 (1948), discussed in Myriad Genetics, 133 S. Ct. at 2117 (explaining that the bacterial mixture of Funk Brothers "was not patent eligible because the patent holder did not alter the bacteria in any way"). While not discussed in the opinion, it is noted that several of the claims held ineligible in Funk Brothers recited specific amounts of the bacterial species in the mixture, *e.g.*, claims 6, 7 and 13. Funk Brothers, 333 U.S. at 128 n.1.

Practice Note: In this set of facts, the specificity of the amounts of each component in this mixture did not result in markedly different characteristics of the sweetener. However, under different facts, other mixtures or combinations with specific amounts may result in markedly different characteristics or, when viewed as a whole, may result in adding significantly more to the claimed product of nature. If that is the case, it would be a best practice to indicate why the claim is eligible by explaining which characteristics are markedly different, and not simply noting that the percentages or ratios do not occur in nature.

Claim 3: Eligible

The claim recites a dietary sweetener comprising 1-5 percent texiol, at least 90 percent water, and 1-2 percent Compound N. Based on the specification's definition of "dietary sweetener", the broadest reasonable interpretation (BRI) of the claim is a mixture of texiol, water, and Compound N in the specified amounts. Because texiol, water, and Compound N are composed of matter, the claim is directed to a statutory category, *e.g.*, a composition of matter (*Step 1*: *YES*).

The claim is then analyzed in Step 2A to determine whether it is directed to any judicial exception. The claimed mixture is a nature-based product that must be compared to its closest naturally occurring counterpart to determine if it has markedly different characteristics than the counterpart. Because texiol, water and Compound N do not occur together in nature, there is no naturally occurring counterpart mixture for comparison. However, texiol does occur naturally in combination with water, in the sap of the Texas mint plant. Accordingly, the closest naturally occurring counterparts to which the claimed mixture is compared are Compound N, and the naturally occurring texiol-water combination. Each of these components is naturally occurring, so none would be eligible

as claimed on its own. There is no indication that mixing these components changes the structure of the components, and no chemical reaction occurs between or among the components. However, the mixture has a changed organoleptic property (*e.g.*, taste), because its flavor profile (sweet and lacking bitterness) is different than the mere sum of the flavors of the individual components, *e.g.*, texiol's sweetness and bitter aftertaste, and Compound N's mild umami flavor. This altered property is a marked difference in characteristics, because it results in the claimed mixture being distinct from its natural counterparts in a way that is relevant to the nature of the invention as a dietary sweetener, *e.g.*, because the taster no longer perceives the bitter aftertaste of naturally occurring texiol. *Cf.* In re Roslin Institute (Edinburgh), 750 F.3d 1333, 1339 (2014) (claimed cloned mammals do not have markedly different characteristics from their naturally occurring counterparts). Thus, the claimed dietary sweetener has markedly different characteristics as compared to its natural counterparts, and is not a "product of nature" exception. Accordingly, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Note that because the analysis of this claim ends in eligibility at Step 2A, the Step 2B analysis is not performed. Thus, the examiner would not need to evaluate the significantly more considerations for this claim. If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

Claim 4: Eligible

The claim recites a dietary sweetener comprising 5 percent texiol, water and/or fruit juice, and sufficient amounts of pectin to provide a solid gel. Based on the specification's definition of "dietary sweetener" and the plain meaning of "solid gel", the broadest reasonable interpretation of the claim is a mixture of texiol, pectin, and water that has the form of a solid gel (*i.e.*, has a jelly-like spreadable consistency). Because the gel is composed of matter, the claim is directed to a statutory category, *e.g.*, a composition of matter (*Step 1*: *YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The claimed gel is a nature-based product that must be compared to its closest naturally occurring counterpart to determine if it has markedly different characteristics than the counterpart. Because texiol, pectin, and water do not occur together in nature (the Texas mint plant does not contain any pectin), there is no naturally occurring counterpart mixture for comparison. However, pectin does occur naturally in combination with water (*e.g.*, in apples), and texiol occurs naturally in combination with water in the thin liquid sap of the Texas mint plant. Accordingly, the closest naturally occurring counterparts to which the claimed gel is compared are the naturally occurring water-pectin and texiol-water combinations. There is no indication that mixing the texiol-water combination with the water-pectin combination changes the structure of the water or pectin. However, the texiol in the claimed mixture does have changed properties as compared to naturally occurring texiol in the plant sap, in that the claimed texiol is present in a solid yet spreadable gel form and has improved organoleptic properties (*e.g.*, a more pleasant mouthfeel). These altered properties are a marked difference in characteristics, because they result in the claimed formulation being distinct from its natural counterparts in a way (jelly-like spreadable consistency and more pleasant mouthfeel) that is relevant to the nature of the invention as a dietary sweetener, *e.g.*, because the claimed formulation can be spread onto other foods such as pastry dough, or formed into candies such as jellybeans. *Cf.* Roslin, 750 F.3d at 1339 (claimed cloned mammals do not have markedly different characteristics from their naturally occurring counterparts). Because the claimed dietary sweetener formulation thus has markedly different characteristics as compared to its natural counterpart, it is not a "product of nature" exception. Accordingly, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Note that because the analysis of this claim ends in eligibility at Step 2A, the Step 2B analysis is not performed. Thus, the examiner would not need to evaluate the significantly more considerations for this claim. If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

Claim 5: Eligible

The claim recites a dietary sweetener comprising granular particles of texiol having a specific particle size distribution, where X10 is 80 microns and X90 is 300 microns. Based on the specification's definition of "dietary sweetener" and the plain meaning of "X10" and "X90", the broadest reasonable interpretation of the claim is a texiol formulation having a specific particle size distribution, *i.e.*, 10 percent of the particles have a diameter smaller than 80 microns, 10 percent of the particles have a diameter greater than 300 microns, and the remaining 80 percent have a diameter between 80 and 300 microns. Because texiol is composed of matter, the claim is directed to a statutory category, *e.g.*, a composition of matter (*Step 1*: *YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The claimed texiol formulation having a specific particle size distribution is a nature-based product that must be compared to its closest naturally occurring counterpart (texiol in its natural irregular crystal state) to determine if it has markedly different characteristics than the counterpart. As disclosed by applicant, the specific particle size distribution results in the claimed texiol formulation having a changed property, *i.e.*, an increased (and consistent) dissolution rate, as opposed to the slow and inconsistent dissolution rate of naturally occurring texiol. This altered property is a marked difference in characteristics, because it results in the claimed formulation being distinct from its natural counterpart in a way (release of sweetness over time) that is relevant to the nature of the invention as a dietary sweetener, *e.g.*, because the claimed formulation will dissolve evenly and rapidly in a cool liquid. *Cf.* Roslin, 750 F.3d at 1339 (claimed cloned mammals do not have markedly different characteristics from their naturally occurring counterparts). Because it has markedly different characteristics as compared to its natural counterpart, the claimed formulation is not a "product of nature" exception. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Note that because the analysis of this claim ends in eligibility at Step 2A, the Step 2B analysis is not performed. Thus, the examiner would not need to evaluate the significantly more considerations for this claim. If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

Claim 6: Eligible

The claim recites a dietary sweetener comprising texiol in a controlled release formulation. Based on the specification's definition of "dietary sweetener" and the plain meaning of "controlled release formulation", the broadest reasonable interpretation of the claim is a texiol formulation that has altered time release properties so that its sweetness is now released in a controlled manner over time due to (a) a change in form or structure or (b) being mixed with other substances (*e.g.*, by being encapsulated in a polymer-emulsifier mixture). In either case, the texiol formulation is composed of matter, and thus the claim is directed to a statutory category, *e.g.*, a composition of matter (*Step 1*: *YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The claimed formulation is a nature-based product that must be compared to its closest naturally occurring counterpart to determine if it has markedly different characteristics than the counterpart. There is

no naturally occurring mixture for comparison, and so the claimed formulation is compared to naturally occurring texiol in its natural state. As disclosed by applicant, the claimed formulation has altered time release properties, in that it releases the sweetness of texiol in a controlled manner over time, as opposed to the naturally occurring texiol, which releases all of its sweetness at one point in time. These altered properties are a marked difference in characteristics, because they result in the claimed formulation being distinct from its natural counterpart in a way (release of sweetness over time) that is relevant to the nature of the invention as a dietary sweetener. *Cf.* Roslin, 750 F.3d at 1339 (claimed cloned mammals do not have markedly different characteristics from their naturally occurring counterparts). Because it has markedly different characteristics as compared to its natural counterpart, the claimed formulation is not a "product of nature" exception. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Note that because the analysis of this claim ends in eligibility at Step 2A, the Step 2B analysis is not performed. Thus, the examiner would not need to evaluate the significantly more considerations for this claim. If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

31. Screening For Gene Alterations

The following illustrates an exemplary analysis using the 2014 IEG for actual claim 1 and hypothetical claims 70, 75, 80, and 85 modeled after the technology in U.S. Patent 5,753,441. Actual claim 1 was held ineligible by the Federal Circuit as directed to an abstract idea without additional elements that amount to significantly more than the abstract idea in Association for Molecular Pathology v. U.S. Patent and Trademark Office, 689 F.3d 1303 (Fed. Cir. 2012) ("Myriad CAFC"), aff'd in part and rev'd in part on other grounds, Association for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107 (2013). (It is noted that claims 7 and 8 of the same patent were held ineligible in University of Utah Research Foundation v. Ambry Genetics Corp., 774 F.3d 755 (Fed. Cir. 2014).) Hypothetical claims 70 and 80 are eligible in Step 2B, because they recite specific and unconventional ways of gathering data that amount to significantly more than the abstract idea, e.g., amplifying nucleic acids via a hypothetical technique known as "Cool-Melt PCR." Hypothetical claims 75 and 85 are eligible in Step 2A, because they are not directed to any judicial exception.

Background

Applicant discovered the "wild-type" sequence of the human BRCA1 gene (*i.e.*, the typical sequence of the gene in humans), and has also discovered naturally occurring alterations from the wild-type sequence that are correlated with an increased likelihood of developing breast or ovarian cancer. Applicant's disclosure provides methods of screening patients for alterations in the BRCA1 gene by comparing a patient's BRCA1 sequence with the wild-type BRCA1 sequence. The compared sequences can be germline (genomic) DNA sequences, RNA sequences, or cDNA sequences.

At the time the invention was made and the application was filed, scientists routinely compared DNA sequences using two data-gathering techniques. The first technique seeks to hybridize two different DNA molecules (*e.g.*, a probe and DNA isolated from a patient sample), and detects whether the molecules bind to each other and form a hybridization product. The second technique amplifies (makes copies of) at least part of a DNA molecule such as DNA isolated from a patient sample, by using a set of primers to produce amplified nucleic acids, and then sequences the amplified nucleic acids. The probes and primers used in these techniques are short single-stranded DNA molecules that typically have a naturally occurring nucleotide sequence, for example a probe to the BRCA1 gene

may have a nucleotide sequence that is identical to a portion of the germline sequence of the wild-type BRCA1 gene.

In one embodiment, applicant discloses using a computer-implemented micromechanical method known as Scanning Near-field Optical Microscopy (SNOM) to detect hybridization of a single probe to its target. SNOM is a technique that achieves high spatial resolution of a nanometric sample, using a laser and optical microscope that are controlled by a computer. At the time the invention was made and the application was filed, the use of SNOM to study DNA hybridization had been discussed in several articles in widely-read scientific journals. However, scientists were not commonly or routinely using SNOM to study DNA hybridization at the time the invention was made and the application was filed. Instead, scientists at the time typically used autoradiography to detect hybridization products.

In another embodiment, applicant discloses using Cool-Melt polymerase chain reaction (Cool-Melt PCR) to amplify BRCA1 DNA from the patient sample. Cool-Melt PCR uses lower melting and annealing temperatures than conventional PCR. Because these lower temperatures result in preferential amplification of mutant nucleic acids as compared to wild-type nucleic acids, Cool-Melt PCR has a 20-fold higher sensitivity of mutation detection than conventional PCR. At the time the invention was made and the application was filed, Cool-Melt PCR was known and used by a few scientists in the field. Several years after filing the application, Cool-Melt PCR became a standard laboratory technique that appeared in virtually every laboratory manual and was conventionally used by most scientists in the field to amplify mutant nucleic acids.

Claims

1. A method for screening germline of a human subject for an alteration of a BRCA1 gene which comprises comparing germline sequence of a BRCA1 gene or BRCA1 RNA from a tissue sample from said subject or a sequence of BRCA1 cDNA made from mRNA from said sample with germline sequences of wild-type BRCA1 gene, wild-type BRCA1 RNA or wild-type BRCA1 cDNA, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA of the subject from wild-type indicates an alteration in the BRCA1 gene in said subject.

70. The method of claim 1, wherein said comparing BRCA1 sequences further comprises:

    hybridizing a wild-type probe to a BRCA1 gene isolated from said sample; and

    detecting the presence of a hybridization product by measuring conformational changes in the probe that are indicative of hybridization to the BRCA1 gene with scanning near-field optical microscopy.

75. A method for hybridizing BRCA1 sequences comprising:

    hybridizing a wild-type probe to a BRCA1 gene isolated from a tissue sample from a human subject; and

    detecting the presence of a hybridization product by measuring conformational changes in the probe that are indicative of hybridization to the BRCA1 gene with scanning near-field optical microscopy.

80. The method of claim 1, wherein said comparing BRCA1 sequences further comprises:

    amplifying by Cool-Melt PCR all or part of a BRCA1 gene from said sample using a set of primers to produce amplified nucleic acids; and

sequencing the amplified nucleic acids.

85. A method for amplifying BRCA1 sequences comprising:

amplifying by Cool-Melt PCR all or part of a BRCA1 gene from a tissue sample from a human subject using a set of primers to produce amplified nucleic acids; and

sequencing the amplified nucleic acids.

Analysis

Claim 1: Ineligible.

The claim recites a step or act, *i.e.*, comparing the patient's genetic sequence with wild type genetic sequences. Thus, the claim is directed to a process, which is one of the statutory categories of invention (*Step 1: YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The claim recites a step of comparing the patient's BRCA1 sequence with wild-type BRCA1 sequences, and a wherein clause stating the result of the comparison, which is that a difference in the compared sequences indicates that the patient has an alteration in the BRCA1 gene. This step of comparing is recited at a high level of generality that merely requires a comparison of two pieces of information and imposes no limits on how the comparison is performed. In *Myriad CAFC*, the court found this step of comparing to be an abstract idea.

When applying the 2014 IEG and interpreting the claim during examination, it is apparent that the step of comparing could be performed by a human using mental steps or basic critical thinking. Similar mental processes have been held by the courts to be abstract ideas, *e.g.*, collecting and comparing known information in Classen, or comparing information regarding a sample or test subject to a control or target data in Ambry and Myriad CAFC. The specific information that is being compared (sequences of a BRCA1 gene, BRCA1 RNA, or BRCA1 cDNA with wild-type sequences) merely narrows the abstract idea, which does not make the comparison step less abstract and is not sufficient to provide eligibility on its own. Thus, the claim is directed to an abstract idea (*Step 2A: YES*).

Note that although nature-based product limitations are recited in the claim (*e.g.*, genes), analysis of the claim as a whole indicates that this claim is focused on a process of comparing information about the products, and is not focused on the products *per se*. Thus, there is no need to perform the markedly different characteristics analysis on the recited nature-based product limitations in this claim.

Next, the claim as a whole is analyzed to determine whether any additional element, or combination of elements, is sufficient to ensure that the claim amounts to significantly more than the abstract idea. The claim recites a single step of comparing, along with a wherein clause, all of which were identified as the abstract idea explained above. There are no other elements/steps recited in the claim. Accordingly, the claim as a whole does not amount to significantly more than the abstract idea of comparing information (*Step 2B: NO*). The claim is not patent eligible.

A rejection of claim 1 should identify the exception by pointing to the comparison of sequences in the claim and explain that this type of comparison of information has been held by the courts to be an abstract idea and that limits on the type of information being compared merely narrow the abstract idea. The rejection should also identify that there are no additional elements/steps in the claim. For clarity, the rejection can explain why the wherein clause does not impose any additional limitations on the claimed method, but merely breathes meaning into the comparison step by stating the result of the comparison.

Claim 70: Eligible

Claim 70 depends from claim 1 and recites at least one step or act, *e.g.*, comparing the patient's genetic sequence with wild type genetic sequences. Thus, the claim is directed to a statutory category of invention (a process; *Step 1: YES*). As a dependent claim, claim 70 incorporates the comparing step of claim 1, which as explained above is an abstract idea. Therefore, the claim is directed to a judicial exception (*Step 2A: YES*).

Next, the claim as a whole is analyzed to determine whether any additional element, or combination of elements, is sufficient to ensure that the claim amounts to significantly more than the exception. Claim 70 recites two additional elements, *i.e.*, that the comparing of claim 1 further comprises a hybridizing step and a detecting step.

The step of hybridizing a wild-type probe to a BRCA1 gene isolated from a sample is recited at a high level of generality, and merely instructs a scientist performing the process to use any hybridization techniques with any probe that she wishes to use to detect any alteration. When recited at this high level of generality, there is nothing in this step that distinguishes it from well-understood, routine and conventional activity engaged in by scientists at the time the invention was made and the application was filed. While this step specifies that the compared sequences are of a probe and a gene, limiting the comparison in this way imposes no limits on how the comparison is performed. Further, it is well established that the mere physical or tangible nature of additional elements such as the hybridizing step does not automatically confer eligibility on a claim directed to an abstract idea (*see*, *e.g.*, Alice Corp. v. CLS Bank Int'l, 134 S.Ct. 2347, 2358-59 (2014)). Thus, taken alone, the hybridizing step does not amount to significantly more.

Claim 70, however, further recites a detecting step in which conformational changes in the gene probe that are indicative of hybridization with the patient's BRCA1 gene are measured by scanning near-field optical microscopy (SNOM). Although SNOM was known to scientists at the time the invention was made and the application was filed, *e.g.*, because it had been discussed in several widely-read scientific journals, mere knowledge of this technique does not make the use of SNOM to detect DNA hybridization routine or conventional in this field. Instead, the evaluation turns on whether the use of SNOM to detect DNA hybridization was actually routinely or conventionally used by scientists at the time the invention was made and the application was filed. Because it was not, the recitation of SNOM to detect DNA hybridization distinguishes claim 70 from well-understood, routine and conventional methods of detecting DNA hybridization such as autoradiography. Thus, the claim's recitation of using SNOM is more than a mere instruction to "apply" the abstract idea using well-understood, routine or conventional techniques in the field. Whether taken alone or as a combination with the other additional elements, the recitation of detecting hybridization using SNOM yields a claim as a whole that is significantly more than the judicial exception itself (*Step 2B: YES*). The claim recites patent eligible subject matter.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance indicating that the claim recites the abstract idea of comparing sequence information. However, the claim is eligible because it recites additional limitations that when considered as a combination are more than a mere instruction to "apply" the abstract idea using well-understood, routine or conventional techniques in the field.

Claim 75: Eligible

Claim 75 recites at least one step or act, *e.g.*, hybridizing a wild-type probe to a BRCA1 gene isolated from a sample. Thus, the claim is directed to a statutory category of invention (a process; *Step 1: YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The claim recites a step of hybridizing a wild-type probe to a BRCA1 gene isolated from a sample and a detecting

step in which conformational changes in the gene probe that are indicative of hybridization with the patient's BRCA1 gene are measured by scanning near-field optical microscopy (SNOM). These steps do not recite or describe any recognized exception. *See, e.g.*, Mayo Collaborative Svcs. v. Prometheus Labs., 566 U.S. __, 132 S. Ct. 1289, 1297 (2012) (recited steps of administering a drug to a patient and determining the resultant level of 6-thioguanine in the patient "are not themselves natural laws"). Accordingly, the claim is not directed to an exception (*Step 2A: NO*), and is eligible.

Note that although nature-based product limitations are recited in the claim (*e.g.*, the probe and BRCA1 gene), analysis of the claim as a whole indicates that the claim is focused on a process of detecting whether the probe has hybridized to the BRCA1 gene, and is not focused on the products *per se*. Thus, there is no need to perform the markedly different characteristics analysis on the recited nature-based product limitations. In addition, note that because the analysis of this claim ends with eligibility at Step 2A, the Step 2B analysis does not need to be performed. Thus, the examiner would not need to evaluate the significantly more considerations for this claim.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

Claim 80: Eligible

Claim 80 depends from claim 1 and recites at least one step or act, *e.g.*, comparing the patient's genetic sequence with wild type genetic sequences. Thus, the claim is directed to a statutory category of invention (a process; *Step 1: YES*). As a dependent claim, claim 80 incorporates the comparing step of claim 1, which as explained above is an abstract idea. Therefore, the claim is directed to a judicial exception (*Step 2A: YES*).

Next, the claim as a whole is analyzed to determine whether any additional element, or combination of elements, is sufficient to ensure that the claim amounts to significantly more than the exception. Claim 80 recites two additional elements, *i.e.*, that the comparing of claim 1 further comprises an amplifying by Cool-Melt PCR step, and a sequencing step.

The step of sequencing the amplified nucleic acids is recited at a high level of generality, and merely instructs a scientist performing the process to use any sequencing technique that she wishes to use. When recited at this high level of generality, there is nothing in this step that distinguishes it from well-understood, routine and conventional activities previously engaged in by scientists in the field at the time the invention was made and the application was filed. Further, it is well established that the mere physical or tangible nature of an additional element such as the sequencing step does not automatically confer eligibility on a claim directed to an abstract idea (*see*, *e.g.*, Alice Corp., 134 S.Ct. at 2358-59).

Claim 80, however, further recites a step in which Cool-Melt PCR is used to amplify the patient's BRCA1 gene. Although Cool-Melt PCR was used by a few scientists in the field to amplify nucleic acids at the time the invention was made and the application was filed, use by only a few scientists does not make the technique routine or conventional in the field as a whole. Nor does it matter that at a later time, Cool-Melt PCR became a routine and conventional technique. Instead, the evaluation turns on whether the use of Cool-Melt PCR to amplify nucleic acids was actually routinely or conventionally used by scientists in this field at the time the invention was made and the application was filed. Because it was not, the recitation of amplification using Cool-Melt PCR distinguishes claim 80 from well-understood, routine and conventional methods of amplification such as standard PCR. Thus, the claim's recitation of amplifying nucleic acids using Cool-Melt PCR is more than a mere instruction to "apply" the abstract idea using well-understood, routine or conventional techniques in the field. Whether taken alone or as a combination with the other additional elements, the recitation of

amplifying using Cool-Melt PCR yields a claim as a whole that is significantly more than the judicial exception itself (*Step 2B: YES*). The claim recites patent eligible subject matter.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance indicating that the claim recites the abstract idea of comparing sequence information. However, the claim is eligible because it recites additional limitations that when considered as a combination are more than a mere instruction to "apply" the abstract idea using well-understood, routine or conventional techniques in the field.

Claim 85: Eligible

Claim 85 recites at least one step or act, *e.g.*, amplifying nucleic acids using Cool-Melt PCR. Thus, the claim is directed to a statutory category of invention (a process; *Step 1: YES*).

The claim is then analyzed to determine whether it is directed to any judicial exception. The claim recites a step of amplifying nucleic acids (all or part of a human subject's BRCA1 gene) using Cool-Melt PCR and a step of sequencing the amplified nucleic acids. These steps do not recite or describe any recognized exception. *See, e.g.*, Mayo Collaborative Svcs. v. Prometheus Labs., 566 U.S. __, 132 S. Ct. 1289, 1297 (2012) (recited steps of administering a drug to a patient and determining the resultant level of 6-thioguanine in the patient "are not themselves natural laws"). Accordingly, the claim is not directed to an exception (*Step 2A: NO*), and is eligible.

Note that although nature-based product limitations are recited in the claim (*e.g.*, the primers and BRCA1 gene), analysis of the claim as a whole indicates that the claim is focused on a process of amplifying and sequencing a BRCA1 gene, and is not focused on the products *per se*. Thus, there is no need to perform the markedly different characteristics analysis on the recited nature-based product limitations. In addition, note that because the analysis of this claim ends with eligibility at Step 2A, the Step 2B analysis does not need to be performed. Thus, the examiner would not need to evaluate the significantly more considerations for this claim.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

32. Paper-Making Machine

This hypothetical example demonstrates the use of the streamlined analysis. The claim below is based on the technology from U.S. Patent 845,224, which was upheld by the Supreme Court in Eibel Process Co. v. Minnesota & Ontario Paper Co., 261 U.S. 45 (1923). As a streamlined analysis would not result in a written rejection, the discussion sets forth exemplary reasoning an examiner might use in drawing a conclusion of eligibility.

Background

Fourdrinier machines are used to make paper from a slurry of wood pulp mixed with water (called "stock"). The paper-forming section of the machines typically comprises a headbox that feeds the stock onto one end of a conveyor belt called a "paper-making wire", which is passed over a series of rolls at a constant speed. The belt carries the stock from the headbox end of the machine (called the "breast-roll end") to the other end (called the "couch-roll end"), while simultaneously draining and shaking the stock to form a continuous paper web. The paper web is then passed into the press section of the machine for further processing.

At the time applicant made the invention and filed the application, it was routine and conventional to arrange the paper-making wire so that the breast-roll end was at the same or a lower height than the couch-roll end, and to feed the stock from the headbox onto the paper-making wire at a speed substantially slower than the wire speed. However, this arrangement necessitated running the machine at an overall slow speed (less than 500 feet/minute) in order to avoid undesirable effects (*e.g*., waves, wrinkles and ripples) on the quality of the paper web.

Applicant's invention is a Fourdrinier machine that solves the problem of running the process at a slow speed by raising the breast-roll end of the paper-making wire to a height substantially above the couch-roll end, and by using gravity to feed the stock into the machine at a speed approximately equal to the wire speed. This gravity-fed arrangement permits applicant's machine to be run at an overall speed that is much higher (*e.g.*, more than 700 feet/minute) than conventional machines, without producing undesirable effects on the quality of the paper web.

Hypothetical Claim

1. A Fourdrinier machine having a breast-roll end of a paper-making wire maintained at a substantial elevation above level, whereby stock is caused to travel by gravity, rapidly, in the direction of movement of the paper-making wire, and at a speed approximately equal to the speed of the paper-making wire.

Analysis

Claim 1: Eligible.

The claim recites a Fourdrinier machine with a paper-making wire (conveyor belt) that is passed over a breast-roll. The claim is directed to a machine (a combination of mechanical parts), which is one of the statutory categories of invention (*Step 1: YES*).

Next, the claim must be evaluated to determine if the claim is directed to a judicial exception. But when the claim is reviewed, it is immediately evident that although the claimed machine operates using gravity, which is a law of nature, the claim clearly does not seek to tie up this law of nature so that others cannot utilize it. In particular, the claim's recitation of a Fourdrinier machine (which is understood in the art to have a specific structure comprising a headbox, a paper-making wire, and a series of rolls) that is arranged in a particular way to optimize the speed of the machine while maintaining quality of the formed paper web makes it clear that the claim as a whole would clearly amount to significantly more than any recited exception. The claim as a whole adds meaningful limitations to the use of the law of nature (gravity). Additionally, use of the law of nature improves paper-making technology. Thus, eligibility of the claim is self-evident for these reasons, and there is no need to perform the full eligibility analysis (*e.g.*, Steps 2A and 2B). The claim is patent eligible.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance indicating that while the claim recites gravity - a law of nature - the claim clearly amounts to significantly more than the mere use of gravity by providing meaningful limitations to the law of nature and additionally improving paper-making technology.

It is noted that although Eibel Process Co. was decided prior to the 1952 Patent Act, the Supreme Court has subsequently described the decision as upholding the eligibility of process claims containing a law of nature. *See, e.g*., Diamond v. Diehr, 450 U.S. 175, 187-88 (1981); Parker v. Flook, 437 U.S. 584, 590-91 and n.12 (1978).

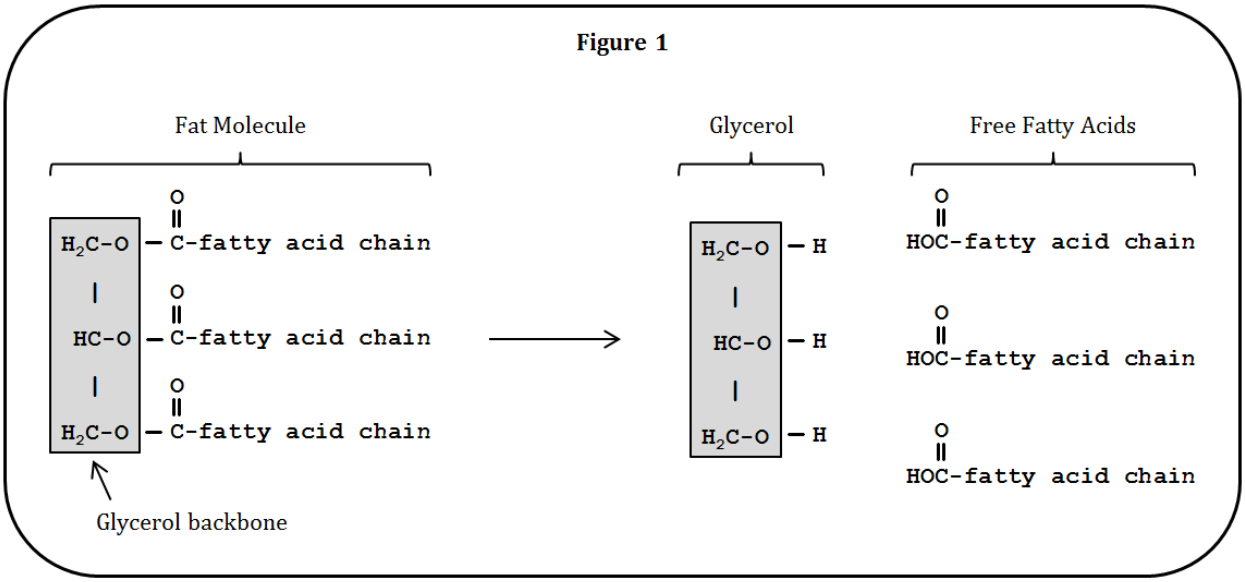
33. Hydrolysis of Fat

This hypothetical example demonstrates the use of the streamlined analysis. The claim below is based on the technology from U.S. Patent 11,766, which was upheld by the Supreme Court in Tilghman v. Proctor, 102 U.S. 707 (1881). As a streamlined analysis would not result in a written rejection, the discussion sets forth exemplary reasoning an examiner might use in drawing a conclusion of eligibility.

Background

Fats are naturally occurring chemicals that are found in many plants and animals, *e.g.*, in tree nuts such as walnuts. As shown in Figure 1, each fat molecule comprises a glycerol backbone to which three fatty acid chains are bound.

Figure 1



As also shown in Figure 1, fat molecules can be broken down into free fatty acids and glycerol (also called glycerine) via a chemical reaction. At the time applicant made the invention and filed the application, it was routine and conventional to carry out this chemical reaction using either the alkaline saponification process, or the sulphuric-acid distillation process. Both of these conventional processes required the use of a steam distillation step in order to produce free fatty acids, and also required the fat to be mixed with either lye or sulphuric acid.

Applicant invented a process of hydrolyzing fat molecules into free fatty acids and glycerol without steam distillation, and using only water as opposed to lye or sulphuric acid. This hydrolysis process begins with a mixture of substantially equal quantities of fat and water in a vessel that is closed and strong enough to resist the effort of the mixture to convert itself into steam. The mixture is then gradually heated to a high temperature (at least 600 degrees Fahrenheit) and kept at that temperature for at least 10 minutes, so that a chemical reaction takes place between the water and fat. While it is heated, the mixture is also subjected to sufficient pressure to prevent the water-fat mixture from forming steam inside the closed vessel.

Hypothetical Claim

1. A process for obtaining free fatty acids and glycerol from fat comprising:

   mixing substantially equal quantities of fat and water in a closed vessel; and

heating the mixture to an elevated temperature of at least 600 degrees Fahrenheit under sufficient pressure to prevent the formation of steam in the closed vessel; and

maintaining the elevated temperature for at least 10 minutes so that the fat and water react with each other to form free fatty acids and glycerol.

Analysis

Claim 1: Eligible.

The claim recites a series of steps for mixing and heating fat and water. Thus, the claim is directed to a process, which is one of the statutory categories of invention (*Step 1: YES*).

Next, the claim must be evaluated to determine if the claim is directed to a judicial exception. But when the claim is reviewed, it is immediately evident that although the claim is founded upon a chemical principle relating to neutral fats, it is not attempting to tie up any judicial exception so that others cannot practice it. In particular, the claim's description of mixing substantially equal quantities of fat and water, heating the mixture to an elevated temperature of at least 600 degrees Fahrenheit under sufficient pressure to prevent the formation of steam in the closed vessel, and maintaining the elevated temperature for at least 10 minutes so that the fat and water react with each other to form free fatty acids and glycerol, makes it clear that the claim as a whole would clearly amount to significantly more than any potential recited exception. For example, the claim as a whole effects a transformation of the fat and water into different chemicals, *i.e.*, from fat and water into the fatty acids and glycerol, by means of specific and unconventional steps. Thus, eligibility of the claim is self-evident in the streamlined analysis, without needing to perform the full eligibility analysis (*e.g.*, Steps 2A and 2B). The claim is patent eligible.

It is important to point out as well that there is no apparent exception recited in the claim, which alone would be sufficient for eligibility. Although the claim is clearly based upon a law of nature (the chemical principle or scientific fact that the elements of neutral fat require that they be severally united with an atomic equivalent of water in order to separate from each other and become free), the law of nature is not recited in the claim. The cases in which courts found claims directed to laws of nature are those in which the law is recited in the claim as part of the invention, such as when the claim sets forth or describes a naturally occurring principle.

If the examiner believes that the record would benefit from clarification, remarks could be added to an Office action or reasons for allowance, indicating that the claim is not directed to any judicial exception.

It is noted that although Tilghman was decided prior to the 1952 Patent Act, the Supreme Court has subsequently described the decision as upholding the eligibility of process claims containing a law of nature. *See, e.g.*, Parker v. Flook, 437 U.S. 584, 590-91 and n.12 (1978); Gottschalk v. Benson, 409 U.S. 63, 70 (1972).