Nature-Based Products

The following examples should be used in conjunction with the 2014 Interim Eligibility Guidance. They replace the examples issued with the March 2014 Procedure For Subject Matter Eligibility Analysis Of Claims Reciting Or Involving Laws Of Nature/Natural Principles, Natural Phenomena, And/Or Natural Products and related training. As the examples are intended to be illustrative only, they should be interpreted based on fact patterns set forth below. Other fact patterns may have different eligibility outcomes.

1. Gunpowder and Fireworks: Product Claims That Are Not Directed To An Exception

This example illustrates the application of the markedly different characteristics analysis to a nature-based product produced by combining multiple components (claim 1), and also provides a sample of a claimed product that when viewed as a whole is not nature-based, and thus is not subjected to the markedly different characteristics analysis in order to determine that the claim is not directed to an exception (claim 2).

Claims:

1. Gunpowder comprising: an intimate finely-ground mixture of 75% potassium nitrate, 15% charcoal and 10% sulfur.
2. A fountain-style firework comprising: (a) a sparking composition, (b) calcium chloride, (c) the gunpowder of claim 1, (d) a cardboard body having a first compartment containing the sparking composition and the calcium chloride and a second compartment containing the gunpowder, and (e) a plastic ignition fuse having one end extending into the second compartment and the other end extending out of the cardboard body.

Analysis of Claims:

These claims are analyzed for eligibility in accordance with their broadest reasonable interpretation. Both claims are directed to a statutory category, *e.g.*, a composition of matter or manufacture (*Step 1: YES*).

Claim 1: Eligible. Because the claim is a nature-based product, *i.e.*, a combination of three naturally occurring substances (potassium nitrate, charcoal and sulfur), the nature-based product (the combination) is analyzed to determine whether it has markedly different characteristics from any naturally occurring counterpart(s) in their natural state. In this case, there is no naturally occurring counterpart to the claimed combination (the components do not occur together in nature), so the combination is compared to the individual components as they occur in nature. None of the three claimed substances are explosive in nature. When the substances are finely-ground and intimately mixed in the claimed ratio, however, the claimed combination is explosive upon ignition. This explosive property of the claimed combination is markedly different from the non-explosive properties of the substances by themselves in nature. Accordingly, the claimed combination has markedly different characteristics, and 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.

Claim 2: Eligible. Although the claim recites two nature-based products (calcium chloride and gunpowder), analysis of the claim as a whole indicates that the claim is focused on the assembly of components that together form the firework, and not the nature-based products. Thus, it is not necessary to apply the markedly different characteristics analysis in order to conclude that the claim is not directed to an exception (*Step 2A: NO)*. The claim qualifies as eligible subject matter.

2. Pomelo Juice: Process Claim That Is Directed To An Exception And Product Claim That Is Not Directed To An Exception

This example illustrates the eligibility analysis of a process (claim 1) that focuses on a nature-based product and a product (claim 2) that is nature-based but is not directed to an exception because it has markedly different characteristics from its naturally occurring counterpart.

Background: The pomelo tree (*Citrus maxima*) is a naturally occurring tree that is native to South and Southeast Asia. Pomelo fruit is often eaten raw or juiced, and has a mild grapefruit-like flavor. Naturally occurring pomelo juice spoils over the course of a few days even when refrigerated, due to the growth of bacteria that are naturally present in the juice. The specification indicates that suitable preservatives for fruit juices are known in the art, and include naturally occurring preservatives such as vitamin E, and non-naturally occurring preservatives such as preservative X. The specification defines an "effective amount" of these preservatives as an amount sufficient to prevent juice from spoiling for at least three weeks, *e.g.*, by retarding the growth of bacteria in the juice.

Claims:

1. A method comprising providing a pomelo fruit.

2. A beverage composition comprising pomelo juice and an effective amount of an added preservative.

Analysis of Claims:

These claims are analyzed for eligibility in accordance with their broadest reasonable interpretation. All of the claims are directed to a statutory category, *e.g.*, a process or composition of matter (*Step 1: YES*).

Claim 1: Ineligible. Although the claim is a process claim, it has been drafted such that there is no difference in substance from a product claim to the pomelo fruit itself. Accordingly, this process claim is focused on the pomelo fruit *per se* (a nature-based product), and must be analyzed for markedly different characteristics, to determine whether the claimed pomelo fruit is a "product of nature" exception. There is no indication in the specification that the claimed fruit has any characteristics (structural, functional, or otherwise) that are different from the naturally occurring fruit provided by pomelo trees. Thus, the claimed fruit does not have markedly different characteristics from what occurs in nature, and is a "product of nature" exception. Accordingly, the claim is directed to an exception (*Step 2A: YES*). Because the claim does not include any additional features that could add significantly more to the exception (*Step 2B: NO*), the claim does not qualify as eligible subject matter, and should be rejected under 35 U.S.C. § 101.

Claim 2: Eligible. Because the claim is a nature-based product, *i.e.*, a combination of a naturally occurring substance (pomelo juice) with an added preservative, the nature-based combination is analyzed to determine whether it has markedly different characteristics from any naturally occurring counterpart(s) in their natural state. In this case, there is no naturally occurring counterpart to the claimed combination, so the combination is compared to the individual components as they occur in nature. The specification indicates that the preservative can be natural or non-natural in origin, but that regardless of its origin, when an effective amount of preservative is mixed with the pomelo juice, the preservative affects the juice so that it spoils much more slowly (spoils in a few weeks) than the naturally occurring juice by itself (spoils in a few days). This property (slower spoiling) of the claimed combination is markedly different from properties of the juice by itself in nature. Accordingly, the claimed combination has markedly different characteristics, and 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.

3. Amazonic Acid, Pharmaceutical Compositions, & Methods of Treatment

This example illustrates the application of the markedly different characteristics analysis to single-element product claims (claims 1, 2 and 3) and to a product-by-process claim (claim 4). It also demonstrates that changes in chemical structure (claims 2 and 3), physical form (claim 5), or chemical/physical properties (claim 6), as compared to a product's natural counterpart can demonstrate markedly different characteristics. Additionally, this example provides samples of claimed processes that when viewed as a whole are not directed to a nature-based product, and thus are not subjected to the markedly different characteristics analysis in order to determine that the claim is not directed to an exception (claims 7 and 8).

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Background: The Amazonian cherry tree is a naturally occurring tree that grows wild in the Amazon basin region of Brazil. The leaves of the Amazonian cherry tree contain a chemical that is useful in treating breast and colon cancers. Many have tried and failed to isolate the cancer-fighting chemical from the leaves. Applicant has successfully purified the cancer-fighting chemical from the leaves and has named it amazonic acid. The purified amazonic acid is structurally and functionally identical to the amazonic acid in the leaves. Applicant has created two derivatives of amazonic acid in the laboratory. The first derivative (called 5-methyl amazonic acid), is structurally different from amazonic acid because a hydrogen has been replaced with a methyl group, and is functionally different because it stimulates the growth of hair in addition to treating cancer. The second derivative (called deoxyamazonic acid), was created by removing a hydroxyl group from amazonic acid and replacing it with a hydrogen. Applicant has not identified any functional difference between deoxyamazonic acid and amazonic acid.

Amazonic acid is absorbed through the lining of the human stomach and is rapidly metabolized by the body. It is also insoluble in water. Applicants disclose an example of a solid pharmaceutical composition demonstrating that when a core of amazonic acid is enveloped by a layer of a natural polymeric material, the resulting manufacture does not release the amazonic acid until it reaches the colon. This colonic release greatly improves the bioavailability of amazonic acid, and is particularly advantageous in the treatment of colon cancer. The specification defines “natural polymeric material” as being a naturally occurring polymer that is not easily digestible by human enzymes, so that it passes through most of the human digestive system intact until it reaches the colon. Specific disclosed examples are shellac and inulin. Applicants disclose an example of an aqueous composition, in which they were able to achieve a stable solution of amazonic acid in water by including a solubilizing agent in the solution. The solubilizing agent can be a naturally occurring product such as a sugar or polyol, or it can be a non-naturally occurring product such as a polysorbate surfactant.

Claims:

1. Purified amazonic acid.
2. Purified 5-methyl amazonic acid.
3. Deoxyamazonic acid.
4. A composition comprising an acid produced by a process which comprises: providing amazonic acid; and replacing the hydroxyl group of the amazonic acid with a hydrogen.
5. A pharmaceutical composition comprising: a core comprising amazonic acid; and a layer of natural polymeric material enveloping the core.
6. A stable aqueous composition comprising: amazonic acid; and a solubilizing agent.
7. A method of treating colon cancer, comprising: administering a daily dose of purified amazonic acid to a patient suffering from colon cancer for a period of time from 10 days to 20 days, wherein said daily dose comprises about 0.75 to about 1.25 teaspoons of amazonic acid.
8. A method of treating breast or colon cancer, comprising: administering an effective amount of purified amazonic acid to a patient suffering from breast or colon cancer.

Analysis of Claims:

These claims are analyzed for eligibility in accordance with their broadest reasonable interpretation. All of the claims are directed to a statutory category, *e.g.*, a composition of matter or process (*Step 1: YES*). Because claims 1-6 are nature-based products (*e.g.*, amazonic acid, 5-methyl amazonic acid, or deoxyamazonic acid), the markedly different characteristics analysis is used to determine if the nature-based products are exceptions. Although claims 7-8 recite nature-based products (amazonic acid), a full eligibility analysis of these claims is not needed because the claims clearly do not seek to tie up all practical uses of the nature-based products.

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Claim 1: Ineligible. Although applicant has discovered that amazonic acid naturally occurs in the leaves of the Amazonian cherry tree, this discovery does not, by itself, render amazonic acid patent eligible. *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. __, 133 S. Ct. 2107, 2117 (2013) ("*Myriad*"). Instead, the claimed acid is analyzed to determine if separating the acid from its surrounding material in the leaf has resulted in the purified amazonic acid having markedly different characteristics from its naturally occurring counterpart. Based on the limited background information, there is no indication that purified amazonic acid has any characteristics (structural, functional, or otherwise) that are different from naturally occurring amazonic acid. The claim therefore encompasses amazonic acid that is structurally and functionally identical to naturally occurring amazonic acid. Because there is no difference between the claimed and naturally occurring acid, the claimed acid does not have markedly different characteristics from what occurs in nature, and thus is a "product of nature" exception. Accordingly, the claim is directed to an exception (*Step 2A: YES*). Because the claim does not include any additional features that could add significantly more to the exception (*Step 2B: NO*), the claim does not qualify as eligible subject matter, and should be rejected under 35 U.S.C. § 101.

Claim 2: Eligible. The claimed 5-methyl amazonic acid has a different structural characteristic than amazonic acid (its chemical structure is different due to the addition of the 5-methyl group). Because 5-methyl amazonic acid is a unique molecule that is distinct from, and does not prevent others from using, naturally occurring amazonic acid, its different structural characteristic rises to the level of a marked difference. Accordingly, the claimed 5-methyl amazonic acid is not a "product of nature" exception. This conclusion is bolstered by the fact that the different structural characteristic has resulted in a different functional characteristic (the stimulation of hair growth). Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Claim 3: Eligible. The claimed deoxyamazonic acid has a different structural characteristic from amazonic acid (its chemical structure is different due to the removal of a hydroxyl group). Based on the limited background information, this change in structure has not resulted in any different functional characteristics. However, because deoxyamazonic acid is a unique molecule that is distinct from, and does not prevent others from using, naturally occurring amazonic acid, its different structural characteristic rises to the level of a marked difference. Accordingly, the claimed deoxyamazonic acid 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.

Claim 4: Eligible. During examination, a product-by-process claim is not limited to manipulations of the recited steps, but instead is only limited to the structure implied by the steps. In this case, the specification describes that removing a hydroxyl group from amazonic acid and replacing it with a hydrogen results in deoxyamazonic acid. Thus, the acid produced by the claimed process steps is deoxyamazonic acid. As explained with respect to claim 3, deoxyamazonic acid has markedly different characteristics than naturally occurring amazonic acid, and 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.

Claim 5: Eligible. The claim is limited to a particular pharmaceutical composition having two naturally occurring substances physically joined together into a non-natural structure (core of amazonic acid surrounded by a layer of natural polymeric material). The claimed composition thus is structurally different from the naturally occurring substances, and this structural difference results in the claimed composition having different functional characteristics *in vivo* (*e.g.*, amazonic acid is not released until the composition reaches the colon, due to the relative indigestibility of the natural polymeric material, thus increasing the bioavailability of the amazonic acid) than the naturally occurring substances by themselves. These different structural and functional characteristics rise to the level of a marked difference, and accordingly the claimed composition 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.

Claim 6: Eligible. In nature, amazonic acid is insoluble in water. As explained in the specification, however, when amazonic acid is combined with a solubilizing agent, it becomes soluble in water and forms a stable solution. This changed property (solubility) between amazonic acid as a part of the claimed stable aqueous composition and amazonic acid in nature is a marked difference. Accordingly, the claimed composition has markedly different characteristics, and 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.

Claim 7: Eligible. Although the claim recites a nature-based product (amazonic acid), 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 (colon cancer), and not on the product *per se*. Thus, it is not necessary to apply the markedly different characteristics analysis in order to conclude that the claim is not directed to an exception (*Step 2A: NO)*. The claim qualifies as eligible subject matter.

Claim 8: Eligible. Although the claim recites a nature-based product (amazonic acid), 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 (breast or colon cancer), and not on the product *per se*. Thus, it is not necessary to apply the markedly different characteristics analysis in order to conclude that the claim is not directed to an exception (*Step 2A: NO)*. The claim qualifies as eligible subject matter.

4. Purified Proteins

This example illustrates that changes in physical/chemical structure (claims 2-5) as compared to a product's natural counterpart can demonstrate markedly different characteristics, whether or not accompanied by changes in biological/pharmacological function or chemical/physical properties.

Background: Newly discovered *Streptomyces arizoneus* bacteria produce Antibiotic L, which exhibits antibiotic activity in nature (*e.g.*, it kills other bacterial species in its natural environment). Naturally occurring Antibiotic L is a protein that occurs in the form of hexagonal-pyramidal crystals (each crystal has the shape of a six-sided pyramid) that are stored inside the bacteria. The specification describes several processes that yield Antibiotic L having the same hexagonal-pyramidal crystal form as naturally occurring Antibiotic L. The specification also discloses a process that yields purified Antibiotic L in the form of tetrahedral crystals (each crystal has the shape of a tetrahedron or triangular pyramid). The specification discloses that naturally occurring Antibiotic L has the amino acid sequence of SEQ ID NO: 2, and has a bacillosamine N-glycan on residue 49. In the specification, applicants describe recombinant yeast that are able to synthesize Antibiotic L (naturally occurring yeast cannot synthesize Antibiotic L or bacillosamine). Purified Antibiotic L expressed by these recombinant yeast has a high mannose (instead of a bacillosamine) N-glycan on residue 49, and has lower immunogenicity to humans and a different half-life *in vivo* than naturally occurring Antibiotic L. The specification defines "purified Antibiotic L" as only being either Antibiotic L in the tetrahedral crystal form or Antibiotic L having a high mannose N-glycan on residue 49.

Applicants disclose substitution modifications of Antibiotic L, *e.g.*, peptides having one or more amino acids substituted with different amino acids relative to SEQ ID NO: 2. No substitution modifications of Antibiotic L are known to occur in nature. Some of the modifications result in altering the function of the peptide, for example by increasing its ability to penetrate the cell membrane of a target organism. The modified peptides have 90% or greater identity to SEQ ID NO: 2.

Claims:

1. Antibiotic L.
2. Purified Antibiotic L.
3. The Antibiotic L of claim 1, which is in a tetrahedral crystal form.
4. The Antibiotic L of claim 1, which is expressed by recombinant yeast.

5. A purified antibiotic comprising an amino acid sequence that has at least 90% identity to SEQ ID NO: 2 and contains at least one substitution modification relative to SEQ ID NO: 2.

Analysis of Claims:

These claims are analyzed for eligibility in accordance with their broadest reasonable interpretation. Because all of the claims are directed to a statutory category, *e.g.*, a composition of matter (*Step 1: YES*), and are nature-based products (Antibiotic L or a derivative thereof), the markedly different characteristics analysis is used to determine if the nature-based products are exceptions.

Claim 1: Ineligible. As described in the specification, some Antibiotic L produced by the applicants is in its naturally occurring hexagonal-pyramidal crystal form, while other Antibiotic L is in a non-natural form, *e.g.*, tetrahedral crystals. The claim thus encompasses antibiotic that is identical to the natural antibiotic, and antibiotic that is changed. Because there is no difference in characteristics (structural, functional, or otherwise) between the claimed and naturally occurring antibiotic for at least some of the embodiments encompassed by the claim, the claimed Antibiotic L does not have markedly different characteristics from what exists in nature, and thus is a "product of nature" exception. Accordingly, the claim is directed to an exception (*Step 2A: YES*). Because the claim does not include any additional features that could add significantly more to the exception (*Step 2B: NO*), the claim does not qualify as eligible subject matter, and should be rejected under 35 U.S.C. § 101.

Claim 2: Eligible. Based on the specification's definition of purified Antibiotic L, the claim is limited to Antibiotic L in the form of tetrahedral crystals or having a high-mannose N-glycan on residue 49. The claim does not encompass naturally occurring Antibiotic L (which forms hexagonal-pyramidal crystals, and has a bacillosamine N-glycan on residue 49). The claimed antibiotic has particular structural/physical characteristics that are different from the naturally occurring antibiotic (*e.g.*, different crystalline form or different N-glycan). The person of ordinary skill in the art would understand that these structural differences may result in the claimed antibiotic having different functional characteristics (*e.g.*, different powder flow behavior or lower immunogenicity and different half-life) than the naturally occurring antibiotic. These differences rise to the level of a marked difference, and thus the claimed antibiotic 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.

Claim 3: Eligible. The claim is limited to Antibiotic L in the form of tetrahedral crystals, and does not encompass the naturally occurring hexagonal-pyramidal crystals. Although the claimed antibiotic is chemically unchanged from nature, the claimed antibiotic has particular structural/physical characteristics that are different from the naturally occurring antibiotic (*e.g.*, different crystalline form). The person of ordinary skill in the art would understand that these structural differences may result in the claimed antibiotic having different functional characteristics (*e.g.*, powder flow behavior) than the naturally occurring antibiotic. These differences rise to the level of a marked difference, and thus the claimed antibiotic 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.

Claim 4: Eligible. During examination, a product-by-process claim is not limited to manipulations of the recited steps, but instead is only limited to the structure implied by the steps. In this case, the specification describes that Antibiotic L produced by recombinant yeast has a different structure (high-mannose N-glycan) than the natural antibiotic (bacillosamine N-glycan). The claim is therefore limited to a structurally different Antibiotic L having a high-mannose N-glycan. This structural difference results in a change to the properties of the claimed antibiotic (lower immunogenicity and different half-life than the natural antibiotic). These differences rise to the level of a marked difference, and thus the claimed antibiotic 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.

Claim 5: Eligible. The claim is limited to peptides in which the amino acid sequence has at least 90% identity to SEQ ID NO: 2, but has been changed to contain at least one non-naturally occurring substitution modification relative to SEQ ID NO: 2. All of the claimed peptides have different structural characteristics (*e.g.*, one or more amino acids have been changed relative to the natural sequence). Some of the claimed peptides may have different functional characteristics, but at least for some conservative modifications there may be no observable functional difference. Because the structural differences between the claimed peptides and their natural counterparts are enough to ensure that the claim is not improperly tying up the future use of naturally occurring Antibiotic L, they rise to the level of a marked difference, and thus the claimed antibiotic 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.

5. Genetically Modified Bacterium

This example illustrates that a naturally occurring product that is unchanged from its natural state does not have markedly different characteristics (claim 1), but that changes in biological function between a claimed product and its natural counterpart can demonstrate markedly different characteristics (claim 2).

Background: Stable energy-generating plasmids that provide hydrocarbon degradative pathways exist within certain bacteria in nature. Different plasmids provide the ability to degrade different hydrocarbons, *e.g.*, one plasmid provides the ability to degrade camphor, and a different plasmid provides the ability to degrade octane. *Pseudomonas* bacteria are naturally occurring bacteria. Naturally occurring *Pseudomonas* bacteria containing one stable energy-generating plasmid and capable of degrading a single type of hydrocarbon are known. There are no known *Pseudomonas* bacteria in nature that contain more than one stable energy-generating plasmid. In the specification, applicant discloses genetically modifying a *Pseudomonas* bacterium to include more plasmids than are found in a single naturally occurring *Pseudomonas* bacterium.

Claims:

1. A stable energy-generating plasmid, which provides a hydrocarbon degradative pathway.
2. A bacterium from the genus *Pseudomonas* containing therein at least two stable energy-generating plasmids, each of said plasmids providing a separate hydrocarbon degradative pathway.

Analysis of Claims:

These claims are analyzed for eligibility in accordance with their broadest reasonable interpretation. Because both claims are directed to a statutory category, *e.g.*, a manufacture or composition of matter (*Step 1: YES*), and are nature-based products (plasmid or bacterium), the markedly different characteristics analysis is used to determine if the nature-based products are exceptions.

Claim 1: Ineligible. Based on the limited background information, there is no indication that the claimed plasmid has any characteristics (structural, functional, or otherwise) that are different from naturally occurring energy-generating plasmids. Because there is no difference between the claimed and naturally occurring plasmid, the claimed plasmid does not have markedly different characteristics, and thus is a "product of nature" exception. Accordingly, the claim is directed to an exception (*Step 2A: YES*). Because the claim does not include any additional features that could add significantly more to the exception (*Step 2B: NO*), the claim does not qualify as eligible subject matter, and should be rejected under 35 U.S.C. § 101.

Claim 2: Eligible. The claimed bacterium has a different functional characteristic from naturally occurring *Pseudomonas* bacteria, *i.e.*, it is able to degrade at least two different hydrocarbons as compared to naturally occurring *Pseudomonas* bacteria that can only degrade a single hydrocarbon. The claimed bacterium also has a different structural characteristic, *i.e.*, it was genetically modified to include more plasmids than are found in a single naturally occurring *Pseudomonas* bacterium. The different functional and structural characteristics rise to the level of a marked difference, and accordingly the

claimed bacterium 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.

The bacterium of claim 2 was held to be patent-eligible subject matter in *Diamond v. Chakrabarty*, 447 U.S. 303 (1980). Recently, the Supreme Court looked back to this claim as an example of a nature-based product that is patent-eligible because it has markedly different characteristics than naturally occurring bacteria, as explained in *Myriad*, 133 S. Ct. at 2116-17:

> In *Chakrabarty*, scientists added four plasmids to a bacterium, which enabled it to break down various components of crude oil. 447 U. S., at 305, 100 S. Ct. 2204, 65 L. Ed. 2d 144, and n. 1. The Court held that the modified bacterium was patentable. It explained that the patent claim was "not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter--a product of human ingenuity 'having a distinctive name, character [and] use.'" *Id.*, at 309-310, 100 S. Ct. 2204, 65 L. Ed. 2d 144 (quoting *Hartranft v. Wiegmann*, 121 U. S. 609, 615, 7 S. Ct. 1240, 30 L. Ed. 1012 (1887); alteration in original). The *Chakrabarty* bacterium was new "with markedly different characteristics from any found in nature," 447 U. S., at 310, 100 S. Ct. 2204, 65 L. Ed. 2d 144, due to the additional plasmids and resultant "capacity for degrading oil."

6. Bacterial Mixtures

This example illustrates the application of the markedly different characteristics analysis to nature-based product claims produced by combining multiple components.

Background: *Rhizobium* bacteria are naturally occurring bacteria that infect leguminous plants such as clover, alfalfa, beans and soy. Each species of bacteria will only infect certain types of plants, for example *R. meliloti* will only infect alfalfa and sweet clover, and *R. phaseoli* will only infect garden beans. It was assumed in the prior art that all *Rhizobium* species were mutually inhibitive, because prior art combinations of different bacterial species produced an inhibitory effect on each other when mixed together, with the result that their efficiency was reduced. Applicant has discovered that there are particular strains of each *Rhizobium* species that do not exert a mutually inhibitive effect on each other, and that these strains can be isolated and used in mixed cultures. Applicant has also discovered that certain *Rhizobium* species, when mixed together, exhibit biological properties that are different than in nature. For example, in nature or by itself, *R. californiana* will only infect lupine. When mixed with *R. phaseoli*, however, *R. californiana* will infect both lupine and wild indigo. *R. californiana* and *R. phaseoli* are not known to occur together in nature.

Claims:

1. An inoculant for leguminous plants comprising a plurality of selected mutually non-inhibitive strains of different species of bacteria of the genus *Rhizobium*, said strains being unaffected by each other in respect to their ability to fix nitrogen in the leguminous plant for which they are specific.
2. An inoculant for leguminous plants comprising a mixture of *Rhizobium californiana* and *Rhizobium phaseoli*.

Analysis of Claims:

These claims are analyzed for eligibility in accordance with their broadest reasonable interpretation. Because both claims are directed to a statutory category, *e.g.*, a composition of matter (*Step 1: YES*), and are nature-based products (a mixture of bacteria), the markedly different characteristics analysis is used to determine if the nature-based products are exceptions.

Claim 1: Ineligible. There is no indication in the specification that the claimed mixture of bacteria has any characteristics (structural, functional, or otherwise) that are different from the naturally occurring

bacteria. Thus, the mixture does not have markedly different characteristics from what occurs in nature, and is a "product of nature" exception. Accordingly, the claim is directed to an exception (*Step 2A: YES*). Because the claim does not include any additional features that could add significantly more to the exception (*Step 2B: NO*), the claim does not qualify as eligible subject matter, and should be rejected under 35 U.S.C. § 101.

The inoculant of claim 1 was held to be ineligible subject matter in *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 131 (1948):

> Discovery of the fact that certain strains of each species of these bacteria can be mixed without harmful effect to the properties of either is a discovery of their qualities of non-inhibition. It is no more than the discovery of some of the handiwork of nature and hence is not patentable. The aggregation of select strains of the several species into one product is an application of that newly-discovered natural principle. But however ingenious the discovery of that natural principle may have been, the application of it is hardly more than an advance in the packaging of the inoculants. Each of the species of root-nodule bacteria contained in the package infects the same group of leguminous plants which it always infected. No species acquires a different use. The combination of species produces no new bacteria, no change in the six species of bacteria, and no enlargement of the range of their utility. Each species has the same effect it always had. The bacteria perform in their natural way. Their use in combination does not improve in any way their natural functioning. They serve the ends nature originally provided and act quite independently of any effort of the patentee.

Recently, the Supreme Court looked back to this claim as an example of ineligible subject matter, stating that "the composition was not patent eligible because the patent holder did not alter the bacteria in any way." *Myriad*, 133 S. Ct. at 2117.

Claim 2: Eligible. In nature, *R. phaseoli* only infects garden beans, and *R. californiana* only infects lupine. When mixed together as claimed, the combination now infects a third species of plant: *R. californiana* infects both lupine and wild indigo, but *R. phaseoli* continues to only infect garden beans. The combination of species thus has changed *R. californiana* such that, when combined with *R. phaseoli*, it has a different characteristic (biological function) than it had in nature, *i.e.*, the claimed combination infects a new group of leguminous plants (wild indigo) as compared to the naturally occurring bacteria by themselves. This functional difference rises to the level of a marked difference, and accordingly the claimed mixture is not a "product of nature" exception. Note that unless the examiner can show that this particular mixture of bacteria exists in nature, this mere possibility does not bar the eligibility of this claim. *See, e.g., Myriad*, 133 S. Ct. at 2119 n.8 ("The possibility that an unusual and rare phenomenon *might* randomly create a molecule similar to one created synthetically through human ingenuity does not render a composition of matter nonpatentable" (emphasis in original)). Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

7. Nucleic Acids

This example illustrates that changes in genetic information/structure (claims 2 and 4), or physical structure (claim 3), as compared to a product's natural counterpart can demonstrate markedly different characteristics.

Background: Virginia nightshade is a naturally occurring plant that grows wild in the Shenandoah Valley of Virginia. When damaged, the leaves of Virginia nightshade produce a hormone called Protein W, which activates chemical defenses against herbivores. Protein W is naturally encoded by Gene W, which is part of chromosome 3 in Virginia nightshade and has the nucleic acid sequence disclosed as SEQ ID NO: 1. The specification also discloses substitution modifications of Gene W, *e.g.*, nucleic acids having one or more nucleotide bases that are substituted with different bases relative to SEQ ID NO: 1. For

example, one of the disclosed modifications changes a naturally occurring adenine to a guanine, *e.g.*, the first nine nucleotides are "TAC GGG AAA" in naturally occurring Gene L and "TAC GGG AAG" in the modified nucleic acid. Some of the modifications are silent, meaning that no change occurs in the encoded protein. It is known in the art that some silent modifications affect characteristics of nucleic acid such as transcription rate and splicing, and that some do not. No substitution modifications of Gene W are known to occur in nature. The modified nucleic acids have 90% or greater identity to SEQ ID NO: 1. The specification discloses labeling the nucleic acids, *e.g.*, with a fluorescent or radioactive label.

The specification discloses vectors comprising SEQ ID NO: 1 and a heterologous nucleic acid. The specification defines "heterologous" nucleic acid sequences as nucleic acid sequences that do not naturally occur in Virginia nightshade, *e.g.*, sequences from other plants, bacteria, viruses, or other organisms. Disclosed heterologous nucleic acids include plant viral vectors such as tobacco mosaic virus, and viral promoters such as the cauliflower mosaic virus (CaMV) 35S promoter. The viral promoters cause different expression of Gene W as compared to its natural expression levels in Virginia nightshade, *e.g.*, Gene W is expressed all the time (constitutively) as opposed to only in response to leaf damage.

Claims:

1. Isolated nucleic acid comprising SEQ ID NO: 1.
2. Isolated nucleic acid comprising a sequence that has at least 90% identity to SEQ ID NO: 1 and contains at least one substitution modification relative to SEQ ID NO: 1.
3. The isolated nucleic acid of claim 1, further comprising a fluorescent label attached to the nucleic acid.
4. A vector comprising the nucleic acid of claim 1 and a heterologous nucleic acid sequence.

Analysis of Claims:

These claims are analyzed for eligibility in accordance with their broadest reasonable interpretation. Because all of the claims are directed to a statutory category, *e.g.* a composition of matter (*Step 1: YES*), and are nature-based products (a nucleic acid), the markedly different characteristics analysis is used to determine if the nature-based products are exceptions.

Claim 1: Ineligible. The claimed nucleic acid has a different structural characteristic than naturally occurring Gene W, because the chemical bonds at each end were severed in order to isolate it from the chromosome on which it occurs in nature, but has the same nucleotide sequence as the natural gene. The claimed nucleic acid has no different functional characteristics, *i.e.*, it encodes the same protein as the natural gene. Under the holding of *Myriad*, this isolated but otherwise unchanged nucleic acid is not eligible because it is not different enough from what exists in nature to avoid improperly tying up the future use and study of naturally occurring Gene W. In other words, the claimed nucleic acid is different, but not markedly different, from its natural counterpart in its natural state (Gene W on chromosome 3), and thus is a "product of nature" exception. Accordingly, the claim is directed to an exception (*Step 2A: YES*). Because the claim does not include any additional features that could add significantly more to the exception (*Step 2B: NO*), the claim does not qualify as eligible subject matter, and should be rejected under 35 U.S.C. § 101.

Claim 2: Eligible. The claim is limited to nucleic acids in which the nucleotide sequence has been changed to contain at least one non-naturally occurring substitution modification relative to SEQ ID NO: 1. All of the claimed nucleic acids have different structural characteristics than the naturally occurring nucleic acid, *e.g.*, one or more nucleotides have been changed relative to the natural sequence. Some of the claimed nucleic acids may have different functional characteristics, *e.g.*, they may encode a different protein than the natural gene. Because the structural differences between the claimed nucleic acids and their natural counterparts are enough to ensure that the claim is not improperly tying up the future use of naturally occurring Gene W, they rise to the level of a marked difference, and so the claimed nucleic acids

are not a "product of nature" exception. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Claim 3: Eligible. The claim is limited to a molecule that includes a nucleic acid and a fluorescent label, which combination does not occur in nature as a single molecule. The claimed molecule thus has different structural characteristics than the naturally occurring nucleic acid and label (single molecule vs. two separate molecules). It also has different functional characteristics (the labeled nucleic acid is now fluorescent, whereas the natural gene is not). These differences rise to the level of a marked difference, and so the claimed molecule 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.

Claim 4: Eligible. The claim is limited to vectors comprising a non-natural combination of Gene W (SEQ ID NO: 1) with a sequence from another organism, and thus does not read on the naturally occurring chromosome in Virginia nightshade. This non-natural combination results in the vectors having a different genetic structure and sequence than the naturally occurring nucleic acids, *i.e.*, different structural characteristics. Some of the claimed vectors may have different functional characteristics, depending on the selected heterologous sequence. These differences rise to the level of a marked difference, and so the claimed vector 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.

8. Antibodies

This example illustrates that products created by human manipulation of natural processes (claims 2 and 3), as well as products that are changed in structure as compared to a product's natural counterpart (claims 4 and 5), can have markedly different characteristics.

Background: Newly discovered *Staphylococcus texana* bacteria have an antigen called Protein S on their outer surface. The specification describes the discovery of naturally occurring antibodies to Protein S in mice and wild coyotes living in Texas. No human antibodies to Protein S are naturally occurring. Antibodies have two types of domains: (1) constant domains such as the Fc domain, which are unvarying in antibodies of a particular class (*e.g.*, IgA) within a species; and (2) variable domains comprising complementarity determining regions (CDRs) that bind to an antigen and that vary from antibody to antibody.

The specification describes multiple types of antibodies to Protein S, including:

- murine antibodies, that were created by injecting laboratory mice with Protein S;
- human antibodies, that were created by injecting transgenic mice with Protein S;
- chimeric antibodies (defined as antibodies that have murine variable domains and human constant domains);
- humanized antibodies (defined as antibodies having murine CDRs but are otherwise human); and
- antibodies with variant Fc domains (defined as antibodies having an Fc domain that is engineered to comprise at least one amino acid modification relative to a wild-type Fc domain).

It is well-known in the art that murine antibodies have different constant domains than human and coyote antibodies, and that murine antibodies may cause allergic reactions and anaphylactic shock when administered to humans or coyotes. The specification discloses a particular murine antibody created by applicants, comprising SEQ ID NOs: 7-12 as its six CDR sequences. There is no naturally occurring antibody that has this particular combination of CDR sequences. It is well-known in the art that chimeric and humanized antibodies are less immunogenic to humans than murine antibodies. It is also well-known that antibodies with variant Fc domains may exhibit different characteristics (*e.g.*, increased cytotoxicity and/or serum half-life) than antibodies with wild-type Fc domains.

Claims:

1. An antibody to Protein S.

2. The antibody of claim 1, wherein the antibody is a human antibody.
3. The antibody of claim 1, wherein the antibody is a murine antibody comprising complementarity determining region (CDR) sequences set forth as SEQ ID NOs: 7-12.
4. The antibody of claim 1, wherein the antibody is a chimeric or humanized antibody.
5. The antibody of claim 1, wherein the antibody comprises a variant Fc domain.

Analysis of Claims:

These claims are analyzed for eligibility in accordance with their broadest reasonable interpretation. Because all of the claims are directed to a statutory category, *e.g.*, a composition of matter (*Step 1: YES*), and are nature-based products (an antibody), the markedly different characteristics analysis is used to determine if the nature-based products are exceptions.

Claim 1: Ineligible. As described in the specification, some antibodies to Protein S are naturally occurring in mice and wild coyotes living in Texas, while other antibodies to Protein S (such as chimeric antibodies) have non-natural forms and may contain domains from multiple species. The claim thus encompasses antibodies that are structurally identical to naturally occurring antibodies, and antibodies that are structurally changed. Because there is no difference in characteristics (structural, functional, or otherwise) between the claimed and naturally occurring antibodies for at least some of the embodiments encompassed by the claim, the claimed antibodies do not have markedly different characteristics, and thus are a "product of nature" exception. Accordingly, the claim is directed to an exception (*Step 2A: YES*). Because the claim does not include any additional features that could add significantly more to the exception (*Step 2B: NO*), the claim does not qualify as eligible subject matter, and should be rejected under 35 U.S.C. § 101.

Claim 2: Eligible. The claim is limited to human antibodies to Protein S. No human antibodies to Protein S are naturally occurring. The claimed antibodies have different complementarity determining regions (CDRs) than what exists in nature, and therefore have different structural (*e.g.*, different amino acid sequences and three-dimensional structures) and functional (*e.g.*, bind to different antigens) characteristics. These differences rise to the level of a marked difference, and so the claimed antibodies are not "product of nature" exceptions. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Claim 3: Eligible. The claim is limited to murine antibodies comprising complementarity determining region (CDR) sequences set forth as SEQ ID NOs: 7-12. Some murine antibodies to Protein S occur in nature, and it is possible that nature might randomly create a murine antibody having the CDR sequences of SEQ ID NOs: 7-12. But unless the examiner can show that this particular murine antibody exists in nature, this mere possibility does not bar the eligibility of this claim. *See, e.g., Myriad*, 133 S. Ct. at 2119 n.8 ("The possibility that an unusual and rare phenomenon *might* randomly create a molecule similar to one created synthetically through human ingenuity does not render a composition of matter nonpatentable" (emphasis in original)). Because the claimed antibodies have different CDRs than what exists in nature, they have different structural (*e.g.*, different amino acid sequences and three-dimensional structures) and functional (*e.g.*, bind to different antigens) characteristics. These differences rise to the level of a marked difference, and so the claimed antibodies are not "product of nature" exceptions. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Claim 4: Eligible. The claim is limited to chimeric and humanized antibodies, which are defined as fusion proteins formed by physically fusing together part of a murine antibody (CDRs or variable domains) and part of a human antibody (constant domains). The claimed antibodies have different structural characteristics than natural antibodies, because the combination of murine and human antibody fragments into a single antibody molecule does not exist in nature. There may also be differences in functional characteristics, *e.g.*, chimeric antibodies are typically less immunogenic to humans than murine

antibodies. These differences rise to the level of a marked difference, and so the claimed antibodies are not "product of nature" exceptions. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

Claim 5: Eligible. The claim is limited to antibodies comprising a variant Fc domain, which is defined as an Fc domain that is engineered to comprise at least one amino acid modification relative to a wild-type Fc domain. The claimed antibodies have different structural characteristics (*e.g.*, different amino acid sequences and three-dimensional structures) than natural antibodies, and may also have different functional characteristics (*e.g.*, different cytotoxicity and/or serum half-life). These differences in characteristics rise to the level of a marked difference, and so the claimed antibodies are not "product of nature" exceptions. Thus, the claim is not directed to an exception (*Step 2A: NO*), and qualifies as eligible subject matter.

9. Cells

This example illustrates that a man-made product identical to a naturally occurring product does not have markedly different characteristics (claim 1), but that changes in phenotype caused by human manipulation can result in markedly different characteristics (claims 2 and 3). It also demonstrates the application of the "significantly more" analysis to claims directed to a "product of nature" exception (claims 4 and 5).

Background: Human stem cells are naturally occurring cells that can develop, through a process called differentiation, into many different types of cells, such as cardiac cells, skin cells, and so on. Stem cells have utility in regenerative medicine, which involves repairing diseased tissues or organs. One type of diseased tissue that often needs repair is the heart's pacemaker, which is formed from pacemaker cells that generate electrical impulses to control heart rate. In nature, pacemaker cells can be identified via a protein called marker P located on the cell surface. The pacemaker cells contain genes that are capable of expressing a protein called marker Z, but in nature these genes are never expressed (there are no naturally occurring pacemaker cells that have marker Z on their surface).

Applicant's specification discloses differentiating stem cells into pacemaker cells, for use in regenerating damaged heart tissue. Applicant discloses isolating stem cells from human volunteers, and then culturing those cells in a particular growth medium in the presence of growth factor A, at various temperatures. Isolation does not change the cells in any way, but applicant's culture conditions cause the stem cells to differentiate into pacemaker cells. Some of the man-made pacemaker cells produced by applicant are genetically and phenotypically identical (*e.g.*, express marker P) to naturally occurring pacemaker cells. Other man-made pacemaker cells produced by applicant are genetically identical, but have a different phenotype (*e.g.*, express marker Z and exhibit increased efficiency in utilizing oxygen) than naturally occurring pacemaker cells. Isolation of these man-made cells does not change them in any way.

The increased oxygen utilization efficiency of the pacemaker cells expressing marker Z is advantageous in the regeneration of heart tissue in patients who are recovering from damage to the heart, such as that caused by a myocardial infarction (heart attack). Applicant has discovered that a mixed population of pacemaker cells that is about 10-15% positive for marker Z (*i.e.*, about 10-15% of the cells in the population express marker Z), and about 85-90% positive for marker P (*i.e.*, about 85-90% of the cells in the population express marker P), can be injected into a patient's heart in order to regenerate a pacemaker *in vivo* (in a patient's body). This successful regeneration is possible because the cells interact with each other to affect their growth rates, *e.g.*, the cells expressing marker P grow faster in the mixed population than when they are by themselves. However, a cell population with fewer (or no) cells expressing marker Z is not capable of regenerating a pacemaker, because the cell population is starved of oxygen before it can become established in the patient.

The specification discloses compositions including populations of pacemaker cells in containers, such as flasks and petri dishes, which are routinely and conventionally used in laboratories to hold cells. Also

disclosed are compositions including populations of pacemaker cells in biocompatible three-dimensional scaffolds. The specification defines "biocompatible three-dimensional scaffolds" as being three-dimensional structures constructed of naturally occurring materials (such as polysaccharides or proteins) that are unchanged from their natural state, in which they are associated with non-cardiac cells, but that have been removed from their natural environment. The specification specifically excludes cardiac tissue from the definition of "biocompatible three-dimensional scaffolds". The specification also discloses that compositions including populations of pacemaker cells in the biocompatible three-dimensional scaffolds can be implanted directly into a patient, where they facilitate faster tissue regeneration than when pacemaker cells are implanted by themselves, because the scaffold provides mechanical support for the implanted cells to grow.

Claims:

1. An isolated man-made human pacemaker cell.
2. An isolated man-made human pacemaker cell expressing marker Z.
3. A population of human pacemaker cells, wherein the population is about 10-15% positive for marker Z, and 85-90% positive for marker P.
4. A composition comprising a population of isolated man-made human pacemaker cells in a container.
5. A composition comprising a population of isolated man-made human pacemaker cells in a biocompatible three-dimensional scaffold.

Analysis of Claims:

These claims are analyzed for eligibility in accordance with their broadest reasonable interpretation. All of the claims are directed to a statutory category, *e.g.*, a composition of matter (*Step 1: YES*).

Claim 1: Ineligible. Because the claim is a nature-based product, *i.e.*, a cell, the nature-based product is analyzed to determine whether it has markedly different characteristics from any naturally occurring counterpart(s) in their natural state. As described in the specification, some of the man-made cells are identical to what exists in nature (*e.g.*, same genotype and phenotype), while others are phenotypically different from what exists in nature (*e.g.*, express marker Z and have increased oxygen utilization), and these difference arose due to applicant's efforts. The claim thus encompasses cells that are identical (no difference in characteristics) to naturally occurring cells, and cells that are phenotypically different. Because there is no difference between the claimed and naturally occurring cells for at least some of the embodiments encompassed by the claim, the claimed cells do not have markedly different characteristics, and thus are a "product of nature" exception. *In re Roslin Institute (Edinburgh)*, 750 F.3d 1333, 1338-39 (Fed. Cir. 2014). Accordingly, the claim is directed to an exception (*Step 2A: YES*). Because the claim does not include any additional features that could add significantly more to the exception (*Step 2B: NO*), the claim does not qualify as eligible subject matter, and should be rejected under 35 U.S.C. § 101.

Claim 2: Eligible. The claim is limited to human pacemaker cells that express marker Z, which are nature-based products. No human pacemaker cells expressing marker Z are naturally occurring. As described in the specification, the claimed cells are exact genetic replicas of naturally occurring pacemaker cells, that were produced from naturally occurring stem cells. However, the claimed cells are phenotypically different than natural pacemaker cells, in that they express marker Z and have increased oxygen utilization efficiency. Further, these phenotypic differences were created by applicant's efforts (*e.g.*, by culturing the stem cells in a particular growth medium in the presence of growth factor A, at various temperatures), and were not the work of nature. These phenotypic differences rise to the level of a marked difference, and accordingly the claimed cell 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.

Claim 3: Eligible. The claim is limited to a population of human pacemaker cells, where about 10-15% of the cells express marker Z, and about 85-90% express marker P. Because the claim is a nature-based

product, *i.e.*, a combination of cells, the nature-based product (the population) is analyzed to determine whether it has markedly different characteristics from any naturally occurring counterpart(s) in their natural state. As discussed above with respect to claims 1 and 2, the cells expressing marker Z have markedly different characteristics than naturally occurring cardiac pacemaker cells because of their phenotypic differences, but the cells expressing marker P do not have markedly different characteristics because they are identical to naturally occurring pacemaker cells. However, as described in the specification, when these cells are mixed together in the claimed ratio to form the claimed population, the cells interact with each other to affect their growth rates, *e.g.*, the cells expressing marker P grow faster in the mixed population than when they are by themselves. Naturally occurring pacemaker cells do not grow at this rate in their natural state. This difference in biological properties (rate of cell growth) between the claimed cell population and naturally occurring human pacemaker cells rises to the level of a marked difference, and accordingly the claimed population 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.

Claim 4: Ineligible. Because the claim recites a nature-based product, *i.e.*, the population of cells, the nature-based product is analyzed to determine whether it has markedly different characteristics from any naturally occurring counterpart(s) in their natural state. As explained with respect to claim 1, isolated man-made pacemaker cells do not have markedly different characteristics due to their isolation or human manufacture. There is no indication in the specification that placing the cells in a generic container results in the cells having any characteristics (structural, functional, or otherwise) that are different from the naturally occurring cells in their natural state. Thus, the claimed population of cells does not have markedly different characteristics from what occurs in nature, and is a "product of nature" exception. Accordingly, the claim is directed to an exception (*Step 2A: YES*). 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. Although the claim recites a container, use of a container to hold cells is not only well-understood, routine and conventional activity already engaged in by the scientific community, it is also required for growing and using the cells. Additionally, the claim recites the container at such a high level of generality that it merely tells a scientist to use whatever container she wishes to use. Therefore, the claim as a whole adds nothing significantly more to the "product of nature" itself. Thus, the claim does not amount to significantly more than the judicial exception itself (*Step 2B: NO*). The claim does not qualify as eligible subject matter, and should be rejected under 35 U.S.C. § 101.

Claim 5: Eligible. Because the claim is a nature-based product, *i.e.*, a combination of cells and a scaffold, the nature-based product (the combination) is analyzed to determine whether it has markedly different characteristics from any naturally occurring counterpart(s) in their natural state. As explained with respect to claim 1, isolated man-made pacemaker cells do not have markedly different characteristics due to their isolation or human manufacture. There is also no indication in the specification that placing the cells into a biocompatible three-dimensional scaffold results in the cells or the scaffold having any characteristics (structural, functional, or otherwise) that are different from the naturally occurring cells or scaffold in their natural state. Thus, the claimed population of cells, and the claimed scaffold, do not have markedly different characteristics from what occurs in nature, and are "product of nature" exceptions. Accordingly, the claim is directed to an exception (*Step 2A: YES*). 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. The recitation of the biocompatible three-dimensional scaffold in combination with the pacemaker cells is not required for growing or using the cells, because the cells can be grown or used in other containers, and is not recited at a high level of generality. The addition of the pacemaker cells to the scaffold confines the claim to a particular useful application of the scaffold (repair of cardiac tissue), because the pacemaker cells are not routinely required for all practical uses of the scaffold. Further, the combination of these elements does more than generally link these two judicial exceptions together; as described in the specification, this combination improves the technology of regenerative medicine, by facilitating faster tissue regeneration than when pacemaker cells are implanted

by themselves. Thus, the claim amounts to significantly more than the judicial exception itself (*Step 2B: YES*), and qualifies as eligible subject matter.

10. Food

This example illustrates the difference between a nature-based product claim having multiple components that are unchanged because they are not combined (claim 1), and a nature-based product claim having multiple components that are changed by their combination (claim 2).

Background: Goats are naturally occurring animals that produce milk to feed their young. Humans have consumed goat milk and products made from goat milk (*e.g.*, cheese and yogurt) for centuries. One well-known method of making goat yogurt is to create a starter culture by mixing raw goat milk with bacteria, and then heating the starter culture to about 115 degrees Fahrenheit for several hours so that the bacteria can ferment the milk. The fermentation causes the conversion of lactose (milk sugar) in the goat milk into lactic acid, and this chemical change results in a physical change (the thickened consistency of the yogurt as compared to the goat milk). The lactic acid also makes the yogurt have a tangy flavor. Multiple species of bacteria are known as useful in making yogurt, including *Streptococcus thermophilus* (a naturally occurring bacterial species).

Applicant has discovered a new naturally occurring bacterial species that it named *Lactobacillus alexandrinus*. Goat milk yogurt made with *L. alexandrinus* has a pleasant tangy flavor. Neither *S. thermophilus* nor *L. alexandrinus* occur naturally in goat milk, and these bacteria do not occur together in nature. Applicant has also discovered that when mixed, *S. thermophilus* and *L. alexandrinus* have different properties than either bacteria has alone: (1) the mixed bacteria act synergistically to ferment goat milk at twice the speed than either bacteria can ferment by itself; and (2) the resultant goat yogurt is much lower in fat than either bacteria can produce when used by itself. Applicant discloses compositions comprising a goat milk starter comprising goat milk mixed with *S. thermophilus* and *L. alexandrinus*. Applicant also discloses kits for preparing goat milk yogurt. The kits comprise a separate packet of *S. thermophilus*, and a separate packet of *L. alexandrinus*, and may also comprise instructions for combining the two bacterial species with goat milk to make yogurt.

Claims:

1. A kit for preparing goat milk yogurt comprising: *Streptococcus thermophilus* and *Lactobacillus alexandrinus*.
2. A yogurt starter culture comprising: goat milk mixed with *Streptococcus thermophilus* and *Lactobacillus alexandrinus.*

Analysis of Claims:

These claims have been analyzed for eligibility in accordance with their broadest reasonable interpretation. Because both claims are directed to a statutory category, *e.g.*, a composition of matter (*Step 1: YES*), and are nature-based products (goat milk and/or bacteria), the markedly different characteristics analysis is used to determine if the nature-based products are exceptions.

Claim 1: Ineligible. As described in the specification, both *S. thermophilus* and *L. alexandrinus* are naturally occurring bacteria. There is no indication in the specification that the claimed bacteria have any characteristics (structural, functional, or otherwise) that are different from the naturally occurring bacteria. Because the bacterial species in the kit are not mixed, but instead are separate from each other, their inclusion in the same kit does not change their characteristics. Although the user of the kit may choose to mix the bacteria together at some time in the future, that mixture, which may or may not exist in the future is not a part of the claimed invention. *In re Venezia*, 530 F.2d 956, 958-59 (CCPA 1976). Thus, the bacterial species in the kit do not have markedly different characteristics from their natural counterparts in their natural state, and are "product of nature" exceptions. Accordingly, the claim is directed to an exception (*Step 2A: YES*). Because the claim does not include any additional features that

could add significantly more to the exceptions (*Step 2B: NO*), the claim does not qualify as eligible subject matter, and should be rejected under 35 U.S.C. § 101.

Claim 2: Eligible. As described in the specification, when *S. thermophilus* and *L. alexandrinus* are mixed, the two bacterial species have different characteristics than either species does on its own, *e.g.*, they act together to ferment milk into a lower fat yogurt than either bacteria can produce when individually mixed with the milk. Thus, the mixture of the bacteria and milk has different functional characteristics (lower fat content) than the naturally occurring bacteria (or milk) by itself. These differences rise to the level of a marked difference, and accordingly the claimed starter culture 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.