It isn’t good: Dx case outcomes

Panel: “Diagnostic Tests - Is There Anything Left to Patent?

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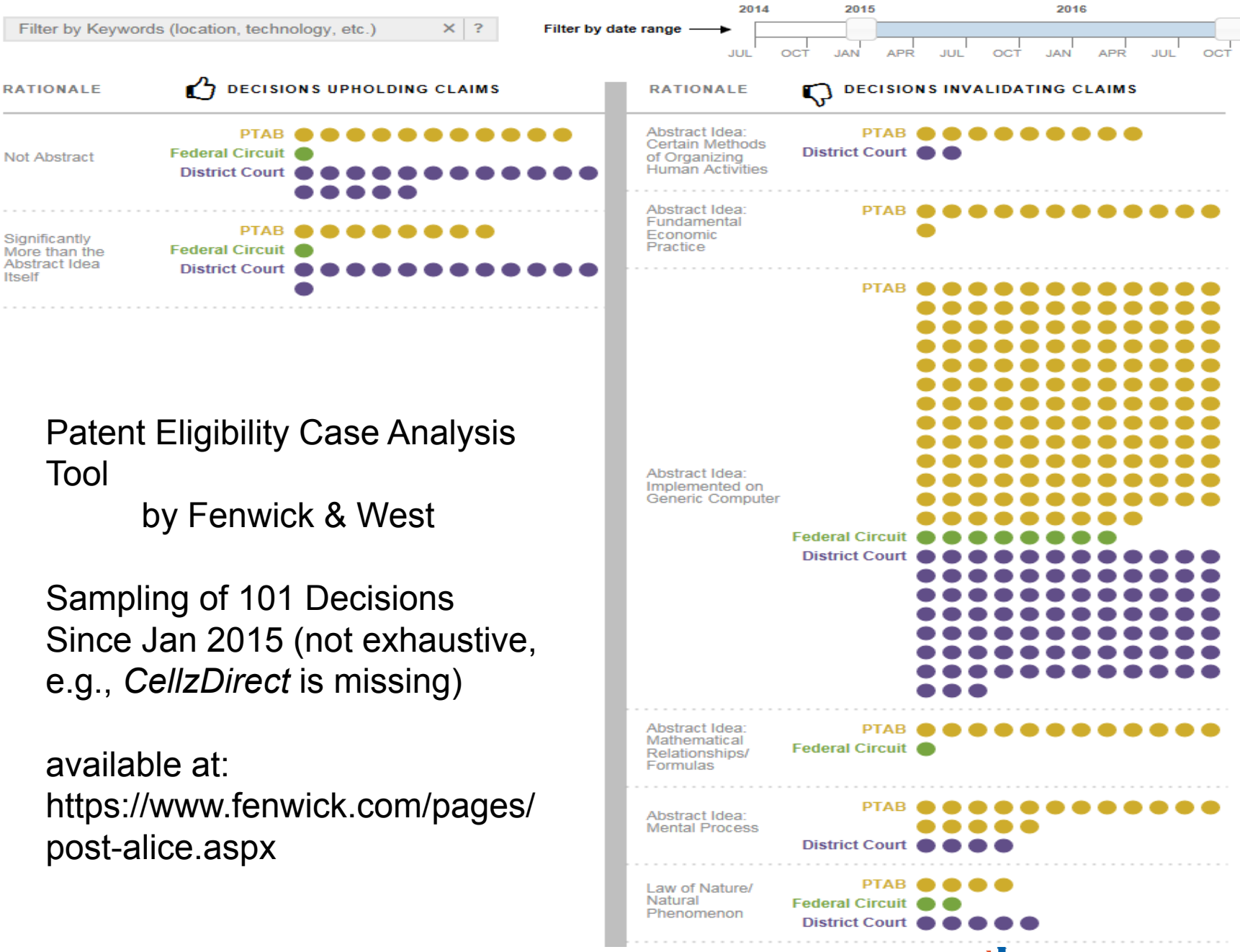

Patent Eligibility Case Analysis Tool

by Fenwick & West

Sampling of 101 Decisions Since Jan 2015 (not exhaustive, e.g., *CellzDirect* is missing)

available at: https://www.fenwick.com/pages/post-alice.aspx

Dx Symp./9.2016/Alexandria /Fischer

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Ameritox, Ltd. V Millenium Health, LLC, **CA No. 13-cv-832-wmc (W. D. Wis., Feb. 18, 2015)**

Abstract Idea? Yes/No! (SJ granted as to '895; denied as to '680)

1. A method for quantifying at least one metabolite in a biological sample comprising the steps of:

(a) providing one biological sample obtained from a patient on a prescribed medication regimen, wherein the sample comprises at least one test metabolite, *wherein in the sample is urine;*

(b) providing one set of known normative data specific to a reference metabolite, wherein the set of data is collected from a population that is on a prescribed medication regimen;

(c) contacting the biological sample with an analytical device;

(d) detecting the presence of at least one test metabolite in the biological sample with the device, wherein the device is capable of measuring the concentration of the test metabolite in the sample;

(e) normalizing the biological sample to adjust for changes in the patient's hydration status by determining the metabolite/creatinine ratio of the patient; and

(f) quantifying the concentration of at least one test metabolite in the biological sample by comparing a ratio between the concentration of the test metabolite from the patient to the set of known normative data specific to the reference metabolite concentration.

('680 patent at 21:9-32.)

Ameritox, Ltd. V Millenium Health, LLC, **CA No. 13-cv-832-wmc (W. D. Wis., Feb. 18, 2015)**

Abstract Idea? Yes/No! (SJ granted as to '895; denied as to '680)

- Step 1(2A) – directed to the comparison of a person's metabolite/creatine ratio to known normative data.
- Step 2(2B) – the claimed invention provides an improvement over existing technology. The *combination* of the normalization, detection and comparison steps were not routine.
  - prior art taught: 1) urine testing gave a + or -, not whether the patient used drug as prescribed; and 2) drug [ ] in urine was too variable, due to hydration and urinary output volume (plasma should be used to measure methadone use).
  - One cannot filter out the comparative step because it is abstract. Nor can one ignore the detection and normalization steps because they exist in the prior art. Instead focus on the entire claim.
  - The '895 claims are not limited to urine. Not only are they overly-broad, but they lack the inventive concept provided by using urine for analysis.

***Genetic Veterinary Sciences Inc. v Canine EIC Genetics, LLC,* CA No. 14-1598 (D. Minn., March 31, 2015)**

Law of Nature? Yes (SJ granted).

1. A method for determining whether a dog has or is predisposed to develop Exercise Induced Collapse (EIC) comprising:

   a) detecting in a nucleic acid sample the allele in the dynamin 1 gene at position 767 of SEQ ID NO: 1, and

   b) identifying that the dog has or is predisposed to the development of EIC when the dog is homozygous for the T767 allele.

***Genetic Veterinary Sciences Inc. v Canine EIC Genetics, LLC,* CA No. 14-1598 (D. Minn., March 31, 2015)**

Law of Nature? Yes (SJ granted).

- Step 1(2A) – directed to observing a genetic mutation tied to a disorder
- Step 2(2B) – the steps are well-understood, routine and conventional, as admitted by the spec.
  - But, some of the dependent claim use very narrow detailed processes to detect
    - CAFC in *BRCA* and *Ariosa* concluded that detailed steps (e.g., for detecting cffDNA or BRCA DNA) do nothing more than spell out what practitioners already know – how to compare gene sequences using routine techniques.
    - Also, the patent identifies the relationship between a specific mutation and a unique disease in dogs. No evidence that other biomarkers may be associated with EIC. The patent narrowly wades into a deep ocean of research and seeks to control all ties between the 767T allele and EIC, rendering it ineligible for protection.

***Endo Pharm Inc. v Actavis Inc.*, CA No. 14-1381-RGA (D. Del. Sept. 23, 2015)**

Law of Nature? Yes (MTD granted).

1. A method of treating pain in a renally impaired patient, comprising the steps of:

a. providing a solid oral controlled release dosage form, comprising:

i. about 5 mg to about 80 mg of oxymorphone or a pharmaceutically acceptable salt thereof as the sole active ingredient; and

ii. a controlled release matrix;

b. measuring a creatinine clearance rate of the patient and determining it to be (a) less than about 30 m[L]/min, (b) about 30 mL/min to about 50 mL/min, (c) about 51 mL/min to about 80 mL/min, or (d) above about 80 mL/min; and

c. orally administering to said patient, in dependence on which creatinine clearance rate is found, a lower dosage of the dosage form to provide pain relief;

wherein after said administration to said patient, the average AUC of oxymorphone over a 12-hour period is less than about 21 ng·hr/mL.[12]

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***Endo Pharm Inc. v Actavis Inc.*, CA No. 14-1381-RGA (D. Del. Sept. 23, 2015)**

Law of Nature? Yes (MTD granted).

- Step 1(2A) – directed to the bioavailabilty of oxy. being increased in people with impaired kidney function.
- Step 2(2B) – "providing" informs the audience of the drug to be administered; "measuring" is routine; "administering" limits the relevant audience and instructs administration of correct dosage.
  - But, the administering step, giving adjusted doses based on kidney impairment, was not routine activity before the invention.
    - This step instructs Dr. to dispense drug in a well-known manner, while using a natural law to manage dosage.
    - And, there are numerous references in the patent that preempt future innovations in the field, e.g., "this invention includes all modifications and equivalents of the subject matter recited in the claims appended hereto as permitted by applicable law. Moreover, any combination of the above described elements in all possible variations thereof is encompassed by the invention".

Esoterix Genetic Lab, LLC v Qiagen LTD., CA No. 14-cv-13228-ADB (D. Mass., Sept. 25, 2015)

Law of Nature? Yes (MTD granted [in part]).

[a] method for determining an increased likelihood of pharmacological effectiveness of treatment by gefitinib or erlotinib in an individual diagnosed with non-small cell lung cancer comprising:

Obtaining DNA from a non-small cell lung cancer tumor sample from the individual; and determining the presence or absence of at least one nucleotide variance in exon 18, 19, or 21 of the epidermal growth factor receptor (EGFR) gene in the DNA, wherein the presence of at least one nucleotide variance selected from:

1) An in-frame deletion in exon 19 of the EGFR gene consisting of a deletion within codons 746 to 753 that results in amino acid changes comprising a deletion of at least amino acids leucine, arginine, and glutamic acid at position 747, 748, and 749 of SEQ ID NO:512;

2) A substitution in exon 21 that results in an amino acid change consisting of a substitution of arginine for leucine at position 858 (L858R) of SEQ ID NO:512, or a substitution in exon 21 that results in an amino acid change consisting of a substitution of glutamine for leucine at position 861 (L861Q) of SEQ ID NO:512; or

3) A substitution in exon 18 that results in an amino acid change consisting of a substitution of cysteine for glycine at position 719 (G719C) of SEQ ID NO:512

indicates an increased likelihood of pharmacological effectiveness of treatment by gefitinib or erlotinib in the individual.

***Esoterix Genetic Lab, LLC v Qiagen LTD.*, CA No. 14-cv-13228-ADB (D. Mass., Sept. 25, 2015)**

Law of Nature? Yes (MTD granted [in part]).

- Step 1(2A) – directed to the correlation between naturally-occurring changes in cancer cells and the likelihood that a drug will work to treat cancer
- Step 2 (2B) – the obtaining and determining steps are entirely conventional, as admitted by the spec.
  - But, it was not conventional to administer these drugs only to patients with these particular genetic mutations.
    - This does not alter or transform a known method of treating cancer, but rather identifies a law of nature that explains why treatment is more effective in certain patients, and tells Drs. to apply that law using well-known methods.

***Cleveland Clinic Found. v True Health Diagnostic, LLC*, CA No. 1:15 CV 2331 (N. D. Ohio, Feb. 23, 2016)**

Law of Nature? Yes (MTD granted)

5. A method of determining whether a patient who presents with chest pain is at risk of requiring medical intervention to prevent an adverse cardiac event within the next six months comprising:

determining the level of risk predictor in a bodily sample from the subject, wherein said risk preddictor is myeloperoxidase activity, myeloperoxidase mass, a myeloperoxidase (MPO)-generated oxidation product or any combination thereof,

wherein said bodily sample is blood, serum, plasma or urine,

wherein said myeloperoxidase-generated oxidation product is nitrotyrosine or a myeloperoxidase-generated lipid peroxidation product selected from [list of products]...or any combination thereof, and

comparing the level of said risk predictor in the bodily sample of the patient to the level of said risk predictor in comparable samples obtained from a control population,

wherein a subject whose bodily sample contains elevated levels of said risk predictor as compared to the control value is at risk of requiring medical intervention to prevent an adverse cardiac event within 6 months of presenting with chest pain.

Cleveland Clinic Found. v True Health Diagnostic, LLC, CA No. 1:15 CV 2331 (N. D. Ohio, Feb. 23, 2016)

Law of Nature? Yes (MTD granted)

- Step 1(2A) – directed to the relationship between MPO levels/activity and the risk of having CV disease
- Step 2(2B) – the remainder of the steps (determining, comparing) are conventional, the spec. even admits this.
  - But, we are the first to "see" MPO by measuring number of molecules and actual activity (prior art "saw" MPO by looking at an intracellular index).
    - You are still measuring naturally occurring levels and activity of MPO.

***Rutgers v Qiagen*, CA No. 1-cv-7187 (D. N.J., Feb. 29, 2016)**

Natural Phenomenon? Not sure (MTD denied)

1. A method of in vitro diagnosis which discriminates between exposure of a subject to Mycobacterium tuberculosis and vaccination with the Bacille Calmette Guerin strain of Mycobacterium bovis, the method comprising

testing for the presence of CD4 T lymphocytes that respond to MTBN4,

wherein the presence of the CD4 T lymphocytes that respond to MTBN4 indicates that the subject has been exposed to Mycobacterium tuberculosis, and

wherein CD4 T lymphocytes from a subject vaccinated with the Bacille Calmette Guerin strain of Mycobacterium bovis but not exposed to Mycobacterium tuberculosis do not respond.

1. A diagnostic composition that discriminates between infection by Mycobacterium tuberculosis and vaccination by Bacille Calmette Guerin (BCG) strain of Mycobacterium bovis, said composition comprising antigens, all antigens in said composition consisting of at least three different polypeptides of the Mycobacterium tuberculosis complex that are not encoded by BCG, and said polypeptides including at least one isolated polypeptide from the group consisting of

(i) a first amino acid sequence consisting of the sequence of MTBN4 (SEQ ID NO: 4),

(ii) a second amino acid sequence that is an antigenic segment of MTBN4 that has Mycobacterium tuberculosis specific antigenic or immunogenic properties and

(iii) a third amino acid sequence that is identical to said first or second amino acid sequence but has conservative substitutions and has Mycobacterium tuberculosis specific antigenic or immunogenic properties.

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***Rutgers v Qiagen*, CA No. 1-cv-7187 (D. N.J., Feb. 29, 2016)**

Natural Phenomenon? Not sure (MTD denied)

- Step 1 (2A) –plausible that not all the materials used in the claimed methods and compositions are naturally-occurring
  - According to Plaintiff, neither the peptide or antigenic segments or its surroundings are naturally occurring and it is illogical that the methods are ineligible simply because they involve elements found in nature.
- Step 2(2B) –plausible that the invention is not simply directed to isolating and identifying materials, but rather applies these materials in a new way to improve a process for detecting TB.
  - The only practical way to diagnose TB before the invention was the TB skin test. The invention is an *in vitro* test done in a single visit giving an objective measurement signifying TB infection.

Idexx Lab., Inc., v. Charles River Lab., Inc., CA No. 15-668-RGA (D. Del., July 1, 2016)

Abstract Idea – No! (MTD denied)

A method of determining a presence or absence of an infectious disease in a population of rodents, the method comprising:

(a) providing a plurality of blood collection cards to a user responsible for a population of animals;

(b) providing instructions to the user comprising the following:

(i) draw blood from an individual rodent;
(ii) apply the blood to one of the plurality of blood collection cards;
(iii) allow the blood sample to dry on the collection card;
(iv) repeat steps i, ii, and iii at least once to provide the plurality of blood collection cards spotted with blood from a plurality of members from the population of rodents; and
(v) transport the plurality of collection cards to a laboratory as a single unit;

(c) receiving the plurality of collection cards as a single unit from the user,

(d) extracting dried blood from the cards;

(e) analyzing the extracted blood for a presence or absence of at least one biological marker for an infectious agent indicative of an infectious disease, thereby determining the presence or absence of the infectious disease in the population; and

(f) reporting the results of the presence or absence of the infectious disease to the user.

***Idexx Lab., Inc., v. Charles River Lab., Inc.*, CA No. 15-668-RGA (D. Del., July 1, 2016)**

Abstract Idea – No! (MTD denied)

- Step 1(2A) – directed to the abstract idea of collecting, analyzing and reporting results
  - NB: claim breadth encouraged the court to broadly construe the AI.
- Step 2(2B) –
  - the individual steps are conventional and routine. But ...
  - As a whole, the steps present a novel implementation of the AI and a clear advance over the prior art (monitoring health of rodent populations without euthanizing, or having to await clotting in a centrifuge, or having to ship in refrigerated containers).
    - "[w]hile the§ 101 inventive concept analysis is facilitated by considerations analogous to those of §§ 102 and 103, it is not a substitute for those statutory requirements. . . .[the reference's] teachings, though possibly relevant to a § 103 determination, fail to demonstrate the lack of an inventive concept."

Vanda Pharmaceuticals Inc. v. Roxane Labs., Inc., CA No. 13-1973 and 14-757 (D. Del., Aug 25, 2016)

Law of Nature? No! (final judgement in favor of Plaintiffs).

A method for treating a patient with iloperidone, wherein the patient is suffering from schizophrenia, the method comprising the steps of: determining whether the patient is a CYP2D6 poor metabolizer by: obtaining or having obtained a biological sample from the patient; and performing or having performed a genotyping assay on the biological sample to determine if the patient has a CYP2D6 poor metabolizer genotype; and if the patient has a CYP2D6 poor metabolizer genotype, then internally administering iloperidone to the patient in an amount of 12 mg/day or less, and if the patient does not have a CYP2D6 poor metabolizer genotype, then internally administering iloperidone to the patient in an amount that is greater than 12 mg/day, up to 24 mg/day, wherein a risk of QTc prolongation for a patient having a CYP2D6 poor metabolizer genotype is lower following the internal administration of 12 mg/day or less than it would be if the iloperidone were administered in an amount of greater than 12 mg/day, up to 24 mg/day.

***Vanda Pharmaceuticals Inc. v. Roxane Labs., Inc.*, CA No. 13-1973 and 14-757 (D. Del., Aug 25, 2016)**

Law of Nature? No! (final judgement in favor of Plaintiffs).

- Step 1(2A) – sparse - "the asserted claims depend upon laws of nature" (relationship between iloperidone, CYP2D6 metabolism, and QTc prolongation).
- Step 2(2B) –dosage step doesn't apply to all patients (only a specific patient population based upon their genetic composition), and requires applying genetic tests in a highly specific way. The use of this genetic test to adjust dosage wasn't routine/conventional, and amounted to more than a mere instruction to apply a natural relationship.
- No preemption issue because claims don't preempt biological sampling or genotyping.

***Oxford Immunotec Ltd. v. Qiagen, Inc.*, CA No. 15-cv-13124-NMG (D. Mass., Aug. 31, 2016)**

Law of Nature? Yes/No! (suggest deny MTD as to method, allow as to kit)

7. A kit for diagnosing infection in a human host by, or exposure of a human host to, a mycobacterium that expresses ESAT-6, comprising a panel of eight peptides represented by SEQ ID NOS: 1 to 8.

1. A method of in vitro diagnosis of *Mycobacterium tuberculosis* infection in a host, comprising
(a) keeping a population of T cells isolated from said host in contact with a peptide panel comprising one or more epitopes contained within peptide SEQ ID NO: 1, and
(b) detecting a recognition response by the T cells to the peptide panel.

Oxford Immunotec Ltd. v. Qiagen, Inc., **CA No. 15-cv-13124-NMG (D. Mass., Aug. 31, 2016)**

Law of Nature? Yes/No! (suggest deny MTD as to method, allow as to kit)

- Step 1(2A) – kit claims: peptides in panel based wholly on natural sequence of ESAT-6; method claims -T-cells previously exposed to *M. tuberculosis* will excrete IFN-γ
- Step 2(2B) – method claims - improve existing methods for diagnosing TB (more convenient, less dependent on a physician's subjective interpretation of results, more accurate); kit claims – only describe peptide panel of test and thus no inventive concept when divorced from the methods.

Your Best Bet?

–Technological Improvement Test –

Thank you!