No. 2010-1406

United States Court of Appeals for the Federal Circuit

THE ASSOCIATION FOR MOLECULAR PATHOLOGY, THE AMERICAN COLLEGE OF MEDICAL GENETICS, THE AMERICAN SOCIETY FOR CLINICAL PATHOLOGY, THE COLLEGE OF AMERICAN PATHOLOGISTS, HAIG KAZAZIAN, MD, ARUPA GANGULY, PHD, WENDY CHUNG, MD, PHD, HARRY OSTRER, MD, DAVID LEDBETTER, PHD, STEPHEN WARREN, PHD, ELLEN MATLOFF, M.S., ELSA REICH, M.S., BREAST CANCER ACTION, BOSTON WOMEN'S HEALTH BOOK COLLECTIVE, LISBETH CERIANI, RUNI LIMARY, GENAE GIRARD, PATRICE FORTUNE, VICKY THOMASON, AND KATHLEEN RAKER,

Plaintiffs-Appellees,

v.

UNITED STATES PATENT AND TRADEMARK OFFICE,

Defendant,

and

MYRIAD GENETICS, INC.,

Defendant-Appellant,

and

LORRIS BETZ, ROGER BOYER, JACK BRITTAIN, ARNOLD B. COMBE, RAYMOND GESTELAND, JAMES U. JENSEN, JOHN KENDALL MORRIS, THOMAS PARKS, DAVID W. PERSHING, AND MICHAEL K. YOUNG, IN THEIR OFFICIAL CAPACITY AS DIRECTORS OF THE UNIVERSITY OF UTAH RESEARCH FOUNDATION,

Defendants-Appellants.

Appeal from the United States District Court for the Southern District of New York in case no. 09-CV-4515, Senior Judge Robert W. Sweet.

CORRECTED BRIEF OF *AMICUS CURIAE* PROTEIN SCIENCES CORPORATION IN SUPPORT OF NEITHER PARTY

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CERTIFICATE OF INTEREST

Counsel for Protein Sciences Corporation certifies the following in accordance with Fed.R.App. 26.1 and Fed.Cir.R. 47.4(a):

1. The full name of every party or *amicus* represented by me is: Protein Sciences Corporation.

2. The name of the real party in interest represented by me is: Protein Sciences Corporation.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or *amicus curiae* represented by me are: None.

4. The names of all law firms and the partners or associates that appeared for the party or *amicus* now represented by me in the trial court or agency or are expected to appear in this Court are: Thomas J. Kowalski, Esq., Deborah L. Lu, PhD, Esq., Robert S, Rigg, Esq. and Vedder Price PC.

Dated: 6/12/12

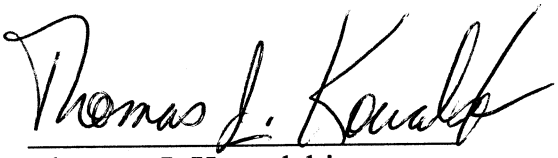

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TABLE OF CONTENTS

Page

CERTIFICATE OF INTEREST i

TABLE OF ABBREVIATIONS iii

STATEMENT OF INTEREST OF *AMICUS CURIAE* PSC AND AUTHORITY TO FILE 1

STATEMENT OF AUTHORSHIP & FUNDING 2

INTRODUCTION AND SUMMARY OF ARGUMENT 2

ARGUMENT 3

I. The Prometheus Test. 3

II. Issue 1: Isolated DNA is Patent Eligible Under Prometheus, Other Law. 6

III. Issue 1: cDNA is Patent Eligible Under Prometheus and Other Law. 10

IV. Issue 2: The Prometheus Test Applied to the Method Claims in Issue. 11

1. The Comparing or Analyzing Claims are not patent eligible under § 101. 12

2. The Growth Rate Claim is § 101 patent eligible because the "transformed cells" are not naturally occurring. 14

V. Conclusion. 15

TABLE OF AUTHORITIES

Page

Cases

Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200 (Fed. Cir. 1991) ..... xii, 6, 9

Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, 653 F.3d 1329 (Fed. Cir. 2011) ..... passim

Bilski v. Kappos, 561 U.S. ___ , 130 S.Ct. 3218 (2010) ..... xi, 4, 5, 6

Diamond v. Chakrabarty, 447 U.S. 303 (1980) ..... xii, 9, 11

Diamond v. Diehr, 450 U.S. 175 (1981) ..... xi, 4, 11, 14

Fiers v.Revel, 984 F.2d 1164 (Fed. Cir. 1993) ..... xii, 6, 9

Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127 (1948) ..... xi, 5, 6, 11

In re Deuel, 53 F.3d 1552 (Fed. Cir. 1995) ..... xii, 6, 9

In re Kubin, 561 F.3d 1351 (Fed. Cir. 2009) ..... xii, 6, 9

In re Ziegler, 992 F.2d 1197 (Fed. Cir. 1993) ..... xi, 5

Mayo Collaborative Services v. Prometheus Laboratories, Inc., 566 U.S. ___, 132 S.Ct 1289 (2012) ..... passim

Parker v. Flook, 437 U.S. 584 (1978) ..... passim

Statutes

35 USC § 101 ..... passim

35 USC § 102 ..... xi, 6

35 USC § 103 ..... xi, 6

35 USC § 112 ..... vi, 5, 6

35 USC § 282 ..... xii, 10

The Leahy-Smith America Invents Act, Public Law 112 – 29 (Sept. 16, 2011) ..... xii, 2, 9

TABLE OF AUTHORITIES
(continued)

Page

Other Authorities

Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office, Case No. 2010-1406 (Fed. Cir., Order, Mar. 26, 2012) ..... xi, 2

Manual of Patent Examining Procedure, Eighth Edition, August 2001, including Latest Revision July 2010 (available at http://www.uspto.gov/web/offices/pac/mpep/index.htm) ..... vii, 6, 10

March 21, 2012 Memorandum of Andrew H. Hirschfeld, Associate Commissioner for Patent Examination Policy, to the United States Patent and Trademark Office Examining Corps (providing guidance on PTO's application of *Prometheus*, available at http://www.uspto.gov/patents/law/exam/mayo_prelim_guidance.pdf) ..... vi, 1

Speech of Hon. Lamar Smith on the AIA, 157 Cong. Rec. E1182-E1185 (daily ed. June 23, 2011) (available at http://www.gpo.gov/fdsys/pkg/CREC-2011-06-23/pdf/CREC-2011-06-23.pdf) ..... xii, 2, 9

The New Shorter Oxford English Dictionary, Vol. I, p. 1544-1545 (Oxford University Press 1993) 5

Rules

Fed.R.App.P. 29(a) 1

Regulations

Utility Examination Guidelines, 66 Fed. Reg. 1092-1099 (Jan. 5, 2001) ..... xii, 9

TABLE OF ABBREVIATIONS	
ABBREVIATION	**EXPLANATION**
Issue 1	What is the applicability of *Prometheus* to the Representative Isolated DNA Claims?
Issue 2	What is the applicability of *Prometheus* to the Growth Rate Claim?
PSC	Protein Sciences Corporation
BARDA	Biomedical Advanced Research and Development Authority (within the Office of the Assistant Secretary for Preparedness and Response in the US Department of Health and Human Services; and Authority that provides an integrated, systematic approach to the development and purchase of the necessary vaccines, drugs, therapies, and diagnostic tools for public health medical emergencies)
HA	Hemagglutinin
FDA	US Food & Drug Administration
NIH	National Institutes of Health
BEVS	Baculovirus Expression Vector System
*expres*SF+®	a unique, FDA-qualified, stable and patented *Spodoptera frugiperda* insect cell line with numerous advantages, including the ability to achieve high density growth and protein expression in serum-free media, without clumping or aggregates
GeneXpress®	PSC's recombinant protein production service that utilizes PSC's proprietary BEVS and *expres*SF+® technologies

TABLE OF ABBREVIATIONS	
ABBREVIATION	**EXPLANATION**
WHO	World Health Organization
FluBlok®	PSC's Phase III BEVS-produced influenza HA anti-influenza vaccine
the '532 patent	US Patent No. 6,245,532
Isolated Nucleic Acid Claims	Claims 2 and 5 of the '532 patent, that read (with claim 2 rewritten in independent form): 2. An isolated nucleic acid encoding the polypeptide [comprising a baculovirus signal peptide comprising amino acids 1-18 of SEQ ID NO: 7 or 9 operatively linked to a heterologous amino acid sequence]. 5. An isolated nucleic acid comprising nucleotides 21-74 of SEQ ID NO: 6 or 8, encoding a baculovirus signal peptide, operatively linked to a heterologous coding sequence.
PTO *Prometheus* Memorandum	March 21, 2012 Memorandum of Andrew H. Hirschfeld, Associate Commissioner for Patent Examination Policy, to the United States Patent and Trademark Office Examining Corps (providing guidance on PTO's application of *Prometheus* (available at http://www.uspto.gov/patents/law/exam/mayo_prelim_guidance.pdf)
Counsel for *amicus curiae* PSC	Thomas J. Kowalski, Esq., Deborah L. Lu, PhD, Esq., and Robert S. Rigg, of Vedder Price PC and Vedder Price PC
§ 101	35 USC § 101
§ 112	35 USC § 112

TABLE OF ABBREVIATIONS	
ABBREVIATION	**EXPLANATION**
A__	Joint Appendix page(s) ___
DNA	Deoxyribonucleic Acid
PTO	United States Patent & Trademark Office
MPEP	Manual of Patent Examining Procedure, Eighth Edition, August 2001, including Latest Revision July 2010 (available at http://www.uspto.gov/web/offices/pac/mpep/index.htm)
US	United States
the ’282 patent	US Patent No. 5,747,282
the ’492 patent	US Patent No. 5,837,492
the ’473 patent	US Patent No. 5,693,473
the ’999 patent	US Patent No. 5,709,999
the ’001 patent	US Patent No. 5,710,001
the ’441 patent	US Patent No. 5,753,441
the ’857 patent	US Patent No. 6,033,857
the Claims in Issue	Claims 1, 2, 5, 6, 7, and 20 of the ’282 patent; claims 1, 6, and 7 of the ’492 patent; claim 1 of the ’473 patent; claim 1 of the ’999 patent; claim 1 of the ’001 patent; claim 1 of the ’441 patent; and claims 1 and 2 of the ’857 patent
Representative Composition Claims	Claims including claims 1, 2, and 5 of the ’282 patent:

TABLE OF ABBREVIATIONS	
ABBREVIATION	**EXPLANATION**
	1. An isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2. 2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1. 5. An isolated DNA having at least 15 nucleotides of the DNA of claim 1.
Representative cDNA Claim	Claim 2 of the ’282 patent
Representative Isolated DNA Claims	Claim 1 of the ‘282 patent and claim 5 of the ’282 patent, the latter of which, rewritten in independent form, reads: An isolated DNA having at least 15 nucleotides of [isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2].
the Method Claims in Issue	the Comparing or Analyzing Claims and the Growth Rate Claim
the Comparing or Analyzing Claims	Method claims that include claim 1 of the ’999 and ’001 patents as being representative: 1. A method for detecting a germline alteration in a BRCA1 gene, said alteration selected from the group consisting of the alterations set forth in Tables 12A, 14, 18 or 19 in a human which comprises analyzing a sequence of a BRCA1 gene or BRCA1 RNA from a human sample or analyzing a sequence of BRCA1 cDNA made from mRNA from said human sample with the proviso that said germline alteration is not a deletion

TABLE OF ABBREVIATIONS	
ABBREVIATION	**EXPLANATION**
	of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO:1. '999 patent claim 1. 1. A method for screening a tumor sample from a human subject for a somatic alteration in a BRCA1 gene in said tumor which comprises [] comparing a first sequence selected from the group consisting of a BRCA1 gene from said tumor sample, BRCA1 RNA from said tumor sample and BRCA1 cDNA made from mRNA from said tumor sample with a second sequence selected from the group consisting of BRCA1 gene from a nontumor sample of said subject, BRCA1 RNA from said nontumor sample and BRCA1 cDNA made from mRNA from said nontumor sample, wherein a difference in the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said tumor sample from the sequence of the BRCA1 gene, BRCA1 RNA or BRCA1 cDNA from said nontumor sample indicates a somatic alteration in the BRCA1 gene in said tumor sample. '001 patent claim 1.
the Growth Rate Claim	Claim 20 of the '282 patent: 20. A method for screening potential cancer therapeutics which comprises: growing a transformed eukaryotic host cell containing an altered BRCA1 gene causing cancer in the presence of a compound suspected of being a cancer therapeutic, growing said transformed eukaryotic host cell in the absence of said compound, determining the rate of growth of said host cell in the presence of said compound and the rate of growth of said host cell in the absence of said compound and comparing the growth rate of said host cells, wherein a

TABLE OF ABBREVIATIONS	
ABBREVIATION	**EXPLANATION**
	slower rate of growth of said host cell in the presence of said compound is indicative of a cancer therapeutic.
the *Prometheus* claim	Claim 1 of US Patent No. 6,355,623, was taken as typical in *Prometheus* and reads: A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising: (a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and (b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder, wherein the level of 6-thioguanine less than about 230 pmol per $8x10^8$ red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and wherein the level of 6-thioguanine greater than about 400 pmol per $8x10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.
Prometheus	The March 20, 2012 Slip Opinion in US Supreme Court Appeal No. 10-1150, *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. ___, 132 S.Ct 1289 (2012) (also called *Mayo* in the April 30, 2012 Order of this Court in the above-captioned case)
the *Prometheus* test	(1) Is the claim a method or process claim? If yes, then: (2) Does the method or process call for applying a law of nature? If yes, then:

TABLE OF ABBREVIATIONS	
ABBREVIATION	**EXPLANATION**
	(3) Do the steps of the method or process: (a) Merely call for a particular audience to apply the law of nature or for applying the law of nature in a particular technological environment, or (b) Call for purely conventional or obvious pre-solution activity?
Myriad	*Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, 653 F.3d 1329 (Fed. Cir. 2011) (this Court's July 29, 2011 opinion in the above-captioned case, as officially reported)
Ass'n for Molecular Pathology (Order, Mar. 26, 2012)	*Ass'n for Molecular Pathology v. U.S. Patent & Trademark Office*, Case No. 2010-1406 (Fed. Cir., Order, Mar. 26, 2012)
Bilski	*Bilski v. Kappos*, 561 U.S. ___ , 130 S.Ct. 3218 (2010)
Diehr	*Diamond v. Diehr*, 450 U.S. 175 (1981)
Flook	*Parker v. Flook,* 437 U.S. 584 (1978)
Ziegler	*In re Ziegler,* 992 F.2d 1197 (Fed. Cir. 1993)
§ 102	35 USC § 102
§ 103	35 USC § 103
Funk Bros.	*Funk Bros. Seed Co. v. Kalo Inoculant Co.,* 333 U.S. 127 (1948)

TABLE OF ABBREVIATIONS	
ABBREVIATION	**EXPLANATION**
Chakrabarty	*Diamond v. Chakrabarty,* 447 U.S. 303 (1980)
PTO Utility Guidelines at _____	pages of Utility Examination Guidelines, 66 Fed. Reg. 1092-1099 (Jan. 5, 2001)
Amgen	*Amgen, Inc. v. Chugai Pharm. Co.,* 927 F.2d 1200 (Fed. Cir. 1991)
Deuel	*In re Deuel*, 53 F.3d 1552 (Fed. Cir. 1995)
Kubin	*In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009)
Fiers	*Fiers v.Revel*, 984 F.2d 1164 (Fed. Cir. 1993)
the AIA	the Leahy-Smith America Invents Act, Public Law 112 – 29 (Sept. 16, 2011)
Smith Speech at _____	pages of Speech of Hon. Lamar Smith on the AIA, 157 Cong. Rec. E1182-E1185 (daily ed. June 23, 2011) (available at http://www.gpo.gov/fdsys/pkg/CREC-2011-06-23/pdf/CREC-2011-06-23.pdf)
§ 282	35 USC § 282

STATEMENT OF INTEREST OF *AMICUS CURIAE* PSC AND AUTHORITY TO FILE

PSC is a Delaware Corporation based in Meriden, CT. Founded in 1983, PSC has nearly 30 years of experience and substantial investment in researching and developing vaccines and biopharmaceuticals for the prevention and treatment of a variety of diseases. Generating about $23 Million in annual revenue through licensing or partnering technologies and from its programs, such as *expres*SF+® cells and GeneXpress®, PSC is actively working with the FDA to bring to market FluBlok®. PSC is also actively working with the NIH and the WHO on US and global preparedness for pandemic influenza. In this regard, PSC was awarded a $147 Million BARDA contract that supports its pandemic influenza vaccine development and licensure program. PSC, through its BEVS technology, is also involved in the Phase III clinical development of Diamyd, a diabetes vaccine candidate, and Glybera, a therapy for lipoprotein lipase deficiency. PSC has a particular interest in the issues involved in this appeal. For example, through its extensive research and development activities, PSC has a patent portfolio that includes the ’532 patent. The ’532 patent has, *inter alia*, Isolated Nucleic Acid Claims. Furthermore, with patent applications pending before the PTO, PSC has an interest in the PTO having guidance beyond the PTO *Prometheus* Memorandum in applying *Prometheus* to pending applications. Pursuant to Fed.R.App.P. 29(a), all parties to this appeal have consented to the filing of this *amicus* brief.

STATEMENT OF AUTHORSHIP & FUNDING

Pursuant to Fed.R.App.P. 29(c)(5), this brief was authored by Thomas J. Kowalski, Esq., Deborah L. Lu, PhD, Esq. and Robert S. Rigg, Esq. of Vedder Price PC, and was funded by *amicus curiae* PSC and Counsel for *amicus curiae* PSC. No party or party's counsel authored this brief in whole or in part. No party or party's counsel funded the preparation or submission of this brief. No person other than the *amicus curiae* PSC and Counsel for *amicus curiae* PSC funded the preparation and submission of this brief.

INTRODUCTION AND SUMMARY OF ARGUMENT

After this Court's correct decision in *Myriad*, the US Supreme Court granted the petition for a writ of certiorari, and remanded this case to this Court for further consideration in light of *Prometheus*. *See Ass'n for Molecular Pathology* (Order, Mar. 26, 2012). Nonetheless, the facts pertaining to isolated DNA and cDNA are as discussed in *Myriad*, 653 F.3d at 1335-1339, 1349-1355, 1361-1373; *see also* A3707-3710, A3972, A3973, A4291,and A4324. Moreover, the AIA has now been enacted and the AIA's legislative history further supports the § 101 patent eligibility of isolated DNA molecules and cDNA. *See* Smith Speech at E1183.

As to Issue 1, *Prometheus* applies to method claims and does not change this Court's correct decision as to the Representative Composition Claims, i.e., that isolated DNA molecules and cDNA are patent eligible subject matter under § 101.

As to Issue 2, applying *Prometheus* to the Comparing or Analyzing Claims produces the same result as in *Myriad*. But, because the "transformed cells containing an altered BRCA1 gene causing cancer" are not naturally occurring cells, the growing of those cells in the presence and absence of a putative cancer therapeutic in the Growth Rate Claim cannot be a method calling for applying a law of nature. Accordingly, under *Prometheus*, isolated DNA molecules, cDNA and the Growth Rate Claim are patent eligible under § 101, and the Comparing or Analyzing Claims are patent ineligible under § 101.

ARGUMENT

I. The *Prometheus* Test.

The *Prometheus* claim is a method or process claim. It calls for a method of "optimizing therapeutic efficacy for treatment of" a disorder. The steps call for "administering a drug" that "provid[es]" a metabolite to a subject having the disorder, and "determining the level of [the metabolite] in the subject." *Prometheus*, 132 S. Ct. at 1296. The wherein clauses specify that if the level of the metabolite is less than a particular threshold value, then that indicates a need to increase the amount of drug subsequently administered, and that if the level of the metabolite is greater than another particular threshold value, then that indicates a need to decrease the amount of drug subsequently administered.

The Supreme Court held that:

> Prometheus' patents set forth laws of nature—namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a … drug will prove ineffective or cause harm … [and,] a process [claim] reciting a law of nature [is not patentable] unless that process has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself.

Prometheus, 132 S. Ct. at 1297. In particular, the "administering" step was held to

> simply refer to the relevant audience, namely doctors who treat patients with certain diseases with … drugs [and be within the] prohibition against patenting abstract ideas [that] "cannot be circumvented by attempting to limit the use of the formula to a particular technological environment."

Id. at 9 (citing *Bilski*, 130 S. Ct. at 3230 (quoting *Diehr*, 450 U.S., at 191-192)).

The "determining" step was held to merely, "tell[] the doctor to determine the level of the relevant metabolites in the blood, through whatever process," with methods for determining metabolite levels admitted in the patent to be well known in the art. *See Prometheus*,132 S. Ct. at 1297. And the "wherein" clauses were held to,

> simply tell a doctor about the relevant natural laws, at most adding a suggestion that he should take those laws into account when treating his patient.

Id. Thus, in summarizing the *Prometheus* claim, the Supreme Court stated:

> Beyond picking out the relevant audience … the claim simply tells doctors to (1) measure (somehow) the current level of the relevant metabolite, (2) use particular (unpatentable) laws of nature … and (3) reconsider the drug dosage in light of the law. These instructions add nothing specific to the laws of nature other than what is well-understood, routine, conventional activity, previously engaged in by those in the field.

Id. at 13.

To apply *Prometheus*, that decision can be reduced to the following test:

(1) Is the claim a method or process claim? If yes, then:

(2) Does the method or process call for applying a law of nature? If yes, then:

(3) Do the steps of the method or process:

(a) Merely call for a particular audience to apply the law of nature or for applying the law of nature in a particular technological environment, or

(b) Call for "[p]urely 'conventional or obvious' '[pre]-solution activity'"? *Id*. at 10 (quoting *Flook* and citing *Bilski*).

As to question (2), **The New Shorter Oxford English Dictionary**, Vol. I, p. 1544-1545 (Oxford University Press 1993) defines "law" as:

> … A regularity in the material world … A principle deduced from observation, applicable to a defined group or class of phenomena, and generally expressible by the statement that a particular phenomenon always occurs if certain conditions are present.

Thus, the term "law of nature" in question (2) means a scientific generalization based upon empirical observation. But caution must be exercised in applying this term because, the term can be "vague and malleable infected with … ambiguity and equivocation." *Funk Bros.,* 333 U.S. at 135 (Frankfurter, J. concurring). If the answer to either question (3)(a) or (3)(b) is 'yes', then the method or process fails to be § 101 patent eligible, and fails to meet the requirements of § 112, ¶ 1. *See In re Ziegler*, 992 F.2d at 1200-1201 ("If the application fails as a matter of fact to satisfy … § 101, then the application also fails as a matter of law … under … §

112."); *see also* MPEP § 2107.01 (instructing that § 101 deficiency also creates § 112, ¶ 1, deficiency as, "[c]ourts have also cast the 35 U.S.C. 101/ 35 U.S.C. 112 relationship such that 35 U.S.C. 112 presupposes compliance with 35 U.S.C. 101").[1] Also, if either question (3)(a) or (3)(b) cannot be answered because the record is insufficient to ascertain whether the steps, as of the effective filing date of the method or process claim, lack novelty under § 102 or are obvious under § 103, then the case should be remanded to develop a record as to whether the steps are "[p]urely 'conventional or obvious' '[pre]-solution activity.'" *Prometheus,*132 S. Ct. at 1298 (quoting *Flook* and citing *Bilski*); *see also id*. at 1304 ("[w]e recognize that, in evaluating the significance of additional steps, the § 101 patent-eligibility inquiry and say, the § 102 novelty inquiry might sometimes overlap.").

Accordingly, under *Prometheus* and *Funk Bros.*, patent eligible invention arises from step (3) when the patent claim calls for more than merely applying a law of nature. *See Prometheus*, 132 S. Ct. at 1294; *see also Funk Bros*., at 134-35 (1948) (Frankfurter, J. concurring) ("[invention] must come from the application of the law of nature to a new and useful end.").

II. Issue 1: Isolated DNA is Patent Eligible Under *Prometheus*, Other Law.

No new facts concerning isolated DNA molecules and cDNA have been

[1] Similarly, for this Court to have decided *Kubin*, *Deuel*, *Fiers* and *Amgen*, isolated DNA and cDNA must be § 101 patent eligible subject matter.

adduced since *Myriad*, *Prometheus* or the Supreme Court's remand.[2] Regarding Issue 1 and § 101 patent eligibility, *Prometheus* applies to method claims and thus does not change this Court's correct decision as to the Representative Composition Claims, i.e., that isolated DNA molecules and cDNA are patent eligible subject matter under § 101. And, even if *Prometheus* applies to the Representative Composition Claims, as to Issue 1, isolated DNA and cDNA are each both a "composition of matter" and a "manufacture" under § 101 and hence § 101 patent eligible subject matter, including because:

(1) Isolated DNA molecules are chemical compositions that possess physical, chemical and structural properties that differ from their naturally-occurring counterparts, and are molecules that man must create. *See, e.g.*, *Myriad*, 653 F.3d at 1362 (Moore, J concurring) (describing how T-C structure in isolated DNA is different than T-C in larger A-T-C-G-T molecule); *id*. at 1335-38, 1351-52 (discussing how isolated DNA has markedly distinctive chemical identity from that of native DNA and is synthesized by human intervention; while in contrast to native DNA that is part of the chromosome around which are histone proteins that thereby package the chromosome, and hence native

[2] The basic technology and facts concerning isolated DNA and its § 101 patent eligibility, as set forth in *Myriad*, 653 F.3d at 1335-1339, 1349-1355, and 1361-1373, and the Joint Appendix, at A3707-3710, A3972, A3973, A4291, A4322-A4324, A4412-15, A4418, A4424-25, and A4728-29, remain unchanged.

DNA into chromatin, which is in turn packaged into the chromosomal structure, isolated DNA is free-standing but "[i]t has not been purified by being isolated," as "isolated DNA molecules do not exist … in nature within a physical mixture to be purified"); *see generally* A3707-3710; A3972; A3973. And,

(2) Isolated DNA is different in kind from any composition found in nature and has new properties not shared by its native counterpart, including, isolated DNA can be used as or to create a probe, a diagnostic tool, a primer, and in sequencing. *See, e.g.*, *Myriad*, 653 F.3d at 1363 (Moore, J concurring) ("isolated DNA allows … remov[al of] potentially confounding sequences … [to] focus on … [the] sequence of interest … [and] additional utility … [as] a … fragment of isolated DNA can be used as a primer …"); *see also id.* at 1366; A4322-4324; A4412-15; A4418; A4424-25; A4728-29.

Applying the above *Prometheus* test to the Representative Isolated DNA Claims results in isolated DNA as § 101 patent eligible under *Prometheus*. Regarding questions (1) and (3) of the *Prometheus* test, the Representative Isolated DNA Claims are not method claims. There are no steps in the Representative Isolated DNA Claims. Hence, these claims do not call for purely conventional or obvious activity. Moreover, and with reference to question (2) of the *Prometheus* test, the isolated DNA of the Claims in Issue is not a product of nature or a law of nature and thus, the Representative Isolated DNA Claims do not call for applying a

law of nature.[3]

Isolated DNA is a composition of matter—strings of chemically joined nucleotides that are different than chromosomal DNA found in nature. *See, e.g., Myriad*, 653 F.3d at 1335-38, 1351-52, 1361-1363; *Chakrabarty*, 447 U.S. at 308 (stating that compositions of matter cover "'all compositions of two or more substances and … [include] all composite articles, [including the] results of chemical union…"); *Amgen*, 927 F.2d at 1206 (recognizing that isolated DNA molecules are complex chemicals and affirming patentability). Isolated DNA is also within the definition of "manufacture" because it is a product of complex processes requiring human intervention that is different from anything found in nature. *See, e.g.*, *Chakrabarty*, 447 U.S. at 308 (using a broad construction of "manufacture"); *Myriad*, 653 F.3d at 1361-1363.

That isolated DNA molecules are patent eligible under § 101 also comports with the longstanding practices of the PTO and this Court, *see, e.g*., *Myriad*, 653 F.2d at 1354, 1367-68; *Kubin*; *Deuel*; *Fiers*; *Amgen*; PTO Utility Guidelines, at 1093, 1094, and with Congress' intent in enacting § 33 of the AIA. *See* Smith Speech at E1183 (enumerating *inter alia* that the AIA § 33 should not be construed

[3] The Table of Abbreviations has '282 patent claim 5 written out in independent form demonstrating that because the "at least 15 nucleotides" is also of the claim 1 "isolated DNA" the full length chromosome cannot be included in the claimed subject matter. *Cf. Myriad*, 653 F.3d at 1367 fn. 5.

to limit PTO ability to issue patents claiming "any chemical compound or composition … including but not limited to nucleic acids"), *cf. Myriad* at 1372 (Congressional approval of PTO policy of granting isolated DNA patents). Under *Prometheus* and other law, isolated DNA is § 101 patent eligible.

III. Issue 1: cDNA is Patent Eligible Under *Prometheus* and Other Law.

cDNA is also well-discussed in *Myriad*[4] and the Joint Appendix:

> cDNAs are not natural forms of DNA that are found in the human body. They are synthesized by reverse transcribing mRNA in a laboratory … They are chemical compositions of matter that are chemically, physically and structurally different from naturally occurring genes. … cDNAs are not the same as the gene sequences in the body—they lack the introns that are present in the naturally occurring gene.

A3709. *See generally* A4335-4338, A4331 (cDNA is structurally and functionally different from native DNA and RNA). Applying the above *Prometheus* test to the Representative cDNA Claim[5] obtains the result that cDNA is § 101 patent eligible.

Firstly, and as explained with respect to isolated DNA, claims to cDNA are not method claims, and there are no steps in the representative cDNA claim, and

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[4] *See Myriad*, 653 F.3d at 1338-1339, 1349-1350, 1353, 1363-1364 (basic technology and law concerning cDNA and its § 101 patent eligibility).

[5] *See Myriad*, 653 F.3d at 1349 fn. 5. Even though this Court's April 30, 2012 Order invites a government brief, the government's briefs and oral arguments, *see also* 653 F.3d 1349, 1350 (discussing government's briefing and oral argument), should be disregarded as contrary to public policy. *See* MPEP §1701 (under § 282 every patent is presumed valid and "[p]ublic policy demands that every employee of the [PTO] refuse to express … any opinion as to the validity or invalidity of, or the patentability or unpatentability of any claim in any U.S. patent").

hence the claim does not call for purely conventional or obvious activity. Secondly, the cDNA of the Claims in Issue is not a product of nature or a law of nature, and the Representative cDNA Claim does not call for applying a law of nature. Thirdly, like isolated DNA, cDNA is a composition of matter and within the definition of "manufacture" of § 101. Indeed, it is well understood that cDNAs are not natural forms of DNA that are found in the human body, and are not the same as gene sequences in the body. *See generally* A3709; A4335-4338.

> cDNA is … not one of the "'manifestations of … nature, free to all men and reserved exclusively to none'" that falls outside of the patent system.

Myriad, 653 F.3d at 1364 (Moore, J. concurring) (quoting *Chakrabarty*, 447 U.S. at 309 (quoting *Funk Bros*., 333 U.S. at 130)). cDNA is § 101 patent eligible.

IV. Issue 2: The *Prometheus* Test Applied to the Method Claims in Issue.

This case arises from the chemical–informational duality of DNA and the § 101 implications flowing from this duality. As to Issue 2, the *Prometheus* test is applied to the Growth Rate Claim and the Comparing or Analyzing Claims to show that when the chemical aspect of DNA is indeed involved in a process claim, it is akin to the § 101 patent eligible subject matter of *Diehr* (claim implementing or applying mathematical formula when considered as whole that performs function such as transforming is patent eligible claim). On the other hand, when the informational aspect of DNA is primarily involved in a process claim it is akin to

the § 101 patent ineligible subject matter of *Flook* (claim reciting and essentially seeking to patent mathematical formula in the abstract is patent ineligible).

1. The Comparing or Analyzing Claims are not patent eligible under § 101.

The Comparing or Analyzing Claims essentially have only one step; namely, "analyzing," ('999 patent claim 1) or "comparing," ('001 patent claim 1). In *Myriad*, this Court held that these claims are not patent eligible under § 101. *See Myriad*, 653 F.3d at 1355-1357. The same result is obtained when the above *Prometheus* test is applied.

The Comparing or Analyzing claims call for "detecting a germline alteration," *see* '999 patent claim 1 or "screening … for a somatic alteration." *See* '001 patent claim 1. Germline mutations are inherited, i.e., they occur in the production of the sperm or egg that gives rise to an individual; *see, e.g.,* A1662; A7454, whereas, somatic mutations arise during an individual's life. *See, e.g.*, A1662; A7454. Claim 1 of the '999 patent calls for:

> detecting a germline alteration … selected from … the alterations set forth in Tables 12 A, 14, 18 or 19 … which comprises analyzing a sequence of a BRCA1 gene or BRCA1 RNA … or a sequence of BRCA1 cDNA made from mRNA from a human sample …

And claim 1 of the '001 patent calls for:

> screening a tumor sample … for a somatic alteration … which comprises [] comparing a first sequence … from a tumor sample with a second sequence … from a nontumor sample of said subject … wherein a difference in the sequence … from said tumor sample from

the sequence … from said nontumor sample indicates a somatic alteration.

Applying the above *Prometheus* test to claim 1 of the ’999 patent, question (1) is answered affirmatively as the claim is a method claim. Question (2) is likewise answered affirmatively as the claim calls for applying a law of nature, namely “analyzing” whether the sample has a germline alteration as set forth in the patent’s Tables. Since the means for performing the analysis is not particularly specified, the claim calls for “conventional or obvious” activities in performing the analysis, and question (3) of the above *Prometheus* test is answered affirmatively. Accordingly, claim 1 of the ’999 Patent fails to be patent eligible under *Prometheus* and is akin to the claim held patent ineligible in *Flook*.

Similarly, applying the above *Prometheus* test to claim 1 of the ’001 patent, question (1) is answered affirmatively as the claim is a method claim. Question (2) is likewise answered affirmatively as the claim calls for applying a law of nature, namely “comparing” sequences of tumor and nontumor cells for a somatic alteration. And question (3) is likewise answered affirmatively as the “wherein” clause of the claim does little more that instruct one to apply the law of nature, namely, that a difference between the sequences of the tumor and nontumor cells indicates a somatic alteration. Accordingly, claim 1 of the ’001 patent fails to be patent eligible under *Prometheus*, and is also akin to the claim rejected in *Flook*.

2. The Growth Rate Claim is § 101 patent eligible because the "transformed cells" are not naturally occurring.

The Growth Rate Claim calls for growing,

> Transformed … cells containing an altered BRCA1 gene causing cancer [in the presence and absence of a putative cancer therapeutic,] determining the rate of growth … in the presence … and the absence of [the putative cancer therapeutic and] comparing the growth rate … wherein a slower rate of growth in the presence [of the putative cancer therapeutic] is indicative of a cancer therapeutic.

Applying the *Prometheus* test to this claim obtains the same result as in *Myriad*, 653 F.3d at 1357-1358; namely, that the claim recites patent eligible subject matter. More specifically, question (1) of the *Prometheus* test is answered affirmatively as the claim calls for a method. However, questions (2) and (3) of the *Prometheus* test are answered negatively. "[T]ransformed cells containing an altered BRCA1 gene causing cancer" are not naturally occurring, and hence the growth of those cells, either in the presence or absence of a putative cancer therapeutic is not calling for the application of a law of nature. Likewise, because "transformed cells containing an altered BRCA1 gene causing cancer" are not naturally occurring, the claim is not merely calling for the application of a law of nature in a particular technical environment or purely conventional or obvious activities. Therefore, the Growth Rate Claim is not a method calling for applying a law of nature, and is patent eligible under *Prometheus* and akin to the claim held to be patent eligible in *Diehr*.

V. Conclusion.

When *Prometheus* is applied to this case, the same result that this Court arrived at in *Myriad* is obtained. Under *Prometheus* isolated DNA and cDNA are compositions and manufacture, and are § 101 patent eligible subject matter. The Analyzing and Comparing Claims fail to do more that state a law of nature and ask one to apply that law of nature. Thus, under *Prometheus*, these claims fail to recite § 101 patent eligible subject matter. The Growth Rate Claim is § 101 patent eligible under *Prometheus* because "transformed cells containing an altered BRCA1 gene causing cancer" are not naturally occurring and hence the "growing," "determining," and "comparing" steps are not merely calling for one to apply a law of nature. This Court should enter a Judgment consistent with its previous decision in this case; *see Myriad.*

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CERTIFICATE OF COMPLIANCE

1. This brief complies with the type-volume limitations of Federal Rules of Appellate Procedure 29(d) and 32(a)(7)(B) because it contains 3,809 words, excluding the parts of the brief exempted by Federal Rules of Appellate Procedure 32(a)(7)(B)(iii) and Federal Circuit Rule 32(b).

2. This brief complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type style requirements of Federal Rule of Appellate Procedure 32(a)(6), because it has been prepared in a proportionally spaced typeface using Microsoft Word in Times New Roman 14 point font.

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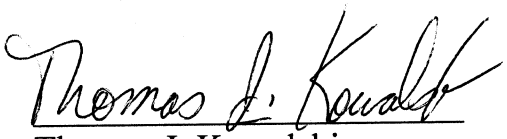

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