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Patent Eligibility of Predictive Algorithm in Second Generation Personalized Medicine

*Jerry I-H Hsiao**

I. INTRODUCTION

Medicine is now undergoing a revolution that will transform its entire practice in every way. This revolution is the result of combining the holistic approach to biology and digital revolution to generate and analyze Big Data.¹ Once realized, we will be moving away from “One-Size-Fits-All” to personalized medicine by recognizing individual differences rather than relying on a statistical average. In past decades, doctors used diagnostic tools to determine if patients carrying certain genes would cause them to be susceptible to certain diseases.² This one-to-one correlation is known as First Generation Personalized Medicine. Now, by combining the power of medicine and computers, doctors are able to use predictive algorithms to diagnose and make treatment decisions using a vast array of data, which is known as Second Generation Personalized Medicine.³

The advent of sophisticated predictive algorithms in Second Generation Medicine needs sufficient incentives. Patents have always provided such incentives for industries to innovate and to disseminate new findings to the public in exchange for a limited monopoly right.⁴ The patent system has played a vital role in promoting the United States as a global innovation powerhouse. However, whether the patent system will continue to serve its role is now called into question by several U.S. Supreme Court cases, including *Mayo Collaborative Services. v. Prometheus Laboratories*⁵ and *Alice Corporation Pty. v. CLS Bank International*.⁶ These two cases, working together, have the potential to deny many useful and valuable process/method inventions at the patent eligibility stage without giving them the chance to be assessed for patentability. To make things worse, *Mayo* and *Alice* give almost no guidance on how one could satisfy the patent eligibility test. A murky

* Assistant Professor in Law, University of Macau; PhD in Law, University of London. I would like to thank members of the SMU Science and Technology Law Review for their dedication and hard work editing this article. All errors are my own.

1. Leroy Hood & Mauricio Flores, *A Personal View on Systems Medicine and the Emergence of Proactive P4 Medicine: Predictive, Preventive, Personalized and Participatory*, 29(6) N. BIOTECHNOLOGY 612 (2013).
2. *How are Genetic Conditions Diagnosed?*, GENETICS HOME REFERENCE (Mar. 19, 2019), <https://ghr.nlm.nih.gov/primer/consult/diagnosis>.
3. Alexander L. Fogel & Joseph C. Kvedar, *Artificial Intelligence Powers Digital Medicine*, DIGITAL MEDICINE 5 (2018).
4. U.S. CONST. art. 1, § 8, cl. 8.
5. 566 U.S. 66 (2012).
6. 573 U.S. 208 (2014).

patent system is not a healthy start for industries focusing on Second Generation Personalized Medicine.

This article aims to assess patent eligibility of the predictive algorithm used in Second Generation Personalized Medicine under *Mayo* and *Alice*. The article first defines the technology behind Second Generation Personalized Medicine in Section II, followed by a look into the patent eligibility jurisprudence in the United States in Section III. The article then assesses the implications that *Mayo* and *Alice* brought to patent eligibility for the predictive algorithm in Section IV and compares the U.S.'s approach to the approach adopted by the European Patent Office (EPO) in Section V. This article then makes recommendations to these judicially-created obstacles in Section VI.

II. REVOLUTION THAT LINKS MEDICINE AND INFORMATION TECHNOLOGY

A. Medical Revolution: The Coming of Systems Medicine

1. Systems Medicine

Systems medicine is the child of systems biology that aims to alter health care through: (1) a systems approach to disease; and (2) driving the emergence of technologies that permit the exploration of new dimensions of patient data space and the analyses of the quantized units of biological information.⁷ Due to their complexity, biological systems cannot be compared to engineered machines, where all parts are exactly known. Instead, biocomplexity needs to be integrative. Hence, system medicine transitioned biology from a rather qualitative and descriptive discipline to a quantitative and explanatory science.⁸

This approach was made possible when biology was equipped with modern analytical technologies, such as omics sciences and a rapid development in computer performance and storage capacity.⁹ The progress in computational, as well as methodological, tools to produce, store and analyze the large amount of biological (genomic, proteomic, metabolomics, or physiomic) data gave rise to the development of mathematical models and computer simulations that are able to describe the underlying dynamics of life processes.¹⁰

7. *Systems Medicine*, WIKIPEDIA, https://en.wikipedia.org/wiki/Systems_medicine (last visited Aug. 26, 2019).

8. Lars Kuepfer & Andreas Schuppert, *Systems Medicine in Pharmaceutical Research and Development*, in *SYSTEMS MEDICINE* 89 (Ulf Schmits & Olaf Wolkenhauer eds., 2016).

9. Marc Kirschner, *Systems Medicine: Sketching the Landscape*, in *SYSTEMS MEDICINE* 5–6 (Ulf Schmits & Olaf Wolkenhauer eds., 2016).

10. *Id.* at 6.

Systems medicine enables the advent of P4 medicine (predictive, preventive, personalized and participatory). In the future, everyone will have his/her genome sequenced.¹¹ The genomes of individuals will provide information on the many genetic variants in the chromosome of each individual to predict the wellness of that individual.¹² Preventive means the ability to predict the potential future emergence of disease-perturbed networks and their cognate diseases.¹³ Personalized means that each person must be treated as a unique individual and not as a statistical average, because humans differ from one another by about six million nucleotides in their genomes.¹⁴ Participatory means that P4 medicine is very different from the passive recipient of expert advice characteristic of pre-digital medicine and relies greatly on the positive contributions of activated patients and consumers.¹⁵ Due to the limited scope of this article, the main focus will be on personalized medicine.

2. From First Generation to Second Generation Personalized Medicine

“Personalized medicine, where Big Data meets Big Health, has been hailed as the next leap forward in health care . . .”¹⁶ Conventional evidence-based medicine relies principally on clinical trials designed to be broadly applicable across populations, so drugs are similarly broadly approved rather than approved for small sub-populations.¹⁷ This approach develops strong scientific evidence of average treatment efficacy but misses much of the variation among patients.¹⁸ Personalized medicine, on the other hand, aims to remedy this problem by demonstrating scientific links between biological patient characteristics, diagnoses, and treatment options.¹⁹

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11. See Megan Humphrey, *Should Everyone Have Their Whole Genome Sequenced at Birth?*, FRONT LINE GENOMICS (Jan. 26, 2018), <http://www.frontlinegenomics.com/news/18759/should-everyone-have-their-whole-genome-sequenced-at-birth/>.
 12. *Id.*
 13. Hood & Flores, *supra* note 1, at 618.
 14. *Id.*
 15. *Id.* at 619.
 16. W. Nicholson Price II, *Black Box Medicine*, 28 HARV. J. L. & TECH. 419, 420 (2015).
 17. Rosemary Roberts et al., *Pediatric Drug Labeling: Improving the Safety and Efficacy of Pediatric Therapies*, JAMA (Aug. 20, 2003), <https://jamanetwork.com/journals/jama/fullarticle/197130>.
 18. P. M. Rothwell, *Can Overall Results of Clinical Trials Be Applied to All Patients?*, 345 LANCET 1616, 1617–18 (1995).
 19. Price, *Black Box Medicine*, *supra* note 16, at 426.

Personalized medicine contrasts with much of contemporary evidence-based medicine.²⁰ The dominant purpose of personalized medicine is to understand the relationship between patient characteristics and interventions which can be validated in clinical trials.²¹ For example, using a single gene test to find whether a patient's cancer is likely to respond to a drug developed alongside that test and treating the patient accordingly is considered First Generation Personalized Medicine.²² One prominent example of this type of medicine was illustrated in Myriad's case.²³ Myriad had discovered the breast cancer gene (BRCA), the gene code for proteins that play a significant role in warding off cancer.²⁴ Some individuals have BRCA genes with variations that attenuate the encoded protein to prevent cancer, thus rendering an individual possessing these variations more susceptible to certain forms of cancer.²⁵ BRCA testing is normally carried out by a clinical laboratory and involves amplifying portions of the patient's DNA by methodologies such as a polymerase chain reaction (PCR).²⁶ The synthetic copies of the genomic DNA molecules resulting from amplification are then analyzed for the presence of genetic variations associated with an altered susceptibility to cancer.²⁷

This simple correlation method fails to address the complexity of biological relationships. This is true especially when "diseases and treatments are frequently dependent on combinations of multiple genetic variables with environmental factors and other physical variables such as weight, blood pressure and sex."²⁸ Aside from the omics data, clinical data could also include demographics, medical notes, electronic recordings from medical devices, physical examinations, and clinical laboratory images.²⁹ All of this data combined (medical Big Data) reached 150 exabytes in the United States

20. *Id.*

21. *Id.*

22. W. Nicholson Price II, *Big Data, Patents, and the Future of Medicine*, 37 CARDOZO L. REV. 1401, 1403 (2016).

23. *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.* 569 U.S. 576 (2013).

24. *Id.* at 576.

25. *Id.* at 582–83.

26. Robert Cook-Deegan et al., *Impact of Gene Patents and Licensing Practices on Access to Genetic Testing for Inherited Susceptibility to Cancer: Comparing Breast and Ovarian Cancers with Colon Cancers*, 12 GENETICS IN MED. S15–16 (2010).

27. *Id.*

28. Price, *Big Data, Patents, and the Future of Medicine*, *supra* note 22, at 1403–04.

29. *Guidance for Industry: Electronic Source Data in Clinical Investigations*, U.S. DEPT. HEALTH & HUMAN SERVS., FOOD & DRUG ADMIN. (Sept. 2013), <https://www.fda.gov/downloads/drugs/guidances/ucm328691.pdf>.

by 2011.³⁰ However, not enough of these data sets have been systematically collected and stored and, therefore, valuable information has not been aggregated, analyzed, or made available in a format to be readily accessed to improve healthcare.³¹ McKinsey Global Institute estimates that the U.S. health care system could save \$300 billion annually if the industry unleashed the full economic potential of data and analytics, which could reduce the national health expenditure by almost eight percent.³² The advent of Second Generation Personalized Medicine could address these challenges by applying artificial intelligence, such as machine learning involving computer algorithms, to detect patterns in data in order to automate complex tasks or make predictions.

B. IT Revolution: The Role of Bioinformatics

1. Bioinformatics

In order to move from First Generation Personalized Medicine to Second Generation Personalized Medicine, the role of medical Big Data cannot be overlooked. This is because the data used to develop the relationships and predictions in treatment recommendations will be much broader and more complicated. It is necessary to characterize the patient at various levels and, consequently, to collect, integrate, and analyze various types of data including clinical data, molecular data, and information about cells, organs, and even social networks.³³ Much of this information is in its raw form and must be analyzed, organized, and stored.³⁴ In order to do so, new computational approaches (bioinformatics) is becoming prominent in biomedical research.³⁵ Nowadays, bioinformatics is defined as “advancing the scientific understanding of living systems through computation” or “conceptualizing biology in terms of molecules and applying” informatics techniques (applied mathemat-

30. *Transforming Health Care Through Big Data*, INST. FOR HEALTH TECH. TRANSFORMATION 5 (2013), http://c4fd63cb482ce6861463-bc6183flc18e748a49b87a25911a0555.r93cf2.rackcdn.com/iHT2_BigData_2013.pdf.

31. *Top 10 Innovations for 2012: #8 Harnessing Big Data to Improve Healthcare*, CLEVELAND CLINIC, <http://innovations.clevelandclinic.org/Summit/Top-10-Medical-Innovations/Top-10-for-2012/8-Harnessing-Big-Data-to-Improve-Healthcare.aspx> (last visited Aug. 26, 2019).

32. Don McDaniel & Dan D’Orazio, *The Changing Role of Analytics for Health Care Providers*, SAGE GROWTH PARTNERS INDUSTRY REP. (Feb. 2012), <https://mk0lemogixesbnriq5w5.kinstacdn.com/wp-content/uploads/2014/12/CHANGING-ROLE-OF-ANALYTICS-FOR-HC-PROVIDERS-FEB-2012.pdf>.

33. Antoine H.C. van Kampen & Perry D. Moerland, *Taking Bioinformatics to Systems Medicine*, in SYSTEMS MEDICINE 18 (Ulf Schmitz & Olaf Wolenhauer eds., 2016).

34. Elizabeth Pennisi, *The Human Genome*, 291 SCIENCE 1177–80 (Feb. 16, 2001).

35. *Spotlight on Bioinformatics*, NATURE.COM (Apr. 6, 2016), <https://www.nature.com/naturejobs/science/articles/10.1038/nj0478>.

ics, computer science, and statistics) to understand and organize the information with these molecules on a large scale.³⁶

Bioinformatics is made up of several components: (1) biological sequences such as DNA, RNA, and protein sequences; (2) databases in which these sequences are organized; and (3) software and hardware designed to create, access, organize, and analyze information contained within these sequences and databases.³⁷ However, this data is meaningless without the algorithm that can give it meaning. As stated earlier, diseases and treatments are frequently dependent on combinations of multiple genetic variables with environmental and other physical factors.³⁸ To find these dependencies and relationships, personalized medicine cannot rely on everything from clinical trials. Instead, scientists can use sophisticated algorithms to analyze large data sets of health information, seeking patterns, predictions, and recommendations.³⁹

2. Predictive Algorithm

Predictive algorithms are applied to find patterns in the data and then to predict medical outcomes and recommend treatment.⁴⁰ Nowadays, predictive algorithms are the result of machine learning. Machine-learning deals with the analysis and development of models and algorithms able to learn from data in order to perform predictive analysis.⁴¹ Depending on whether it incorporates the outcomes, First Generation Machine Learning can be divided into unsupervised,⁴² supervised,⁴³ and semi-supervised.⁴⁴ In the clinical setting, supervised learning is more clinically relevant than unsupervised learning, and unsupervised learning is often used as a part of the preprocessing step to

36. van Kampen & Moerland, *supra* note 33, at 20.

37. M. Scott McBride, *Bioinformatics and Intellectual Property Protection*, 17 BERKELEY TECH. L. 1331, 1334 (2002).

38. Price, *Big Data, Patents, and the Future of Medicine*, *supra* note 22, at 1403–04.

39. *Id.*

40. *Id.* at 1401.

41. Angela Serra et al., *Machine Learning for Bioinformatics and Neuroimaging*, 8 WIRES DATA MINING & KNOWLEDGE DISCOVERY (2018).

42. A machine learning system automatically finds dependencies, correlations, and clusters in the data without requiring any significant human intervention. Steven M. Bellovin et al., *When Enough is Enough: Location Tracking, Mosaic Theory, and Machine Learning*, 8 N.Y.U. J. L. & LIBERTY 555, 591–96 (2014).

43. A machine learning system that requires human annotation effort is suitable for predictive modeling via building some relationship between the patient traits (as input) and the outcome of interest (as output). *Id.* at 592–94.

44. Semi-supervised learning can be seen as the natural blend of both supervised and unsupervised methods. *Id.* at 594–96.

make the follow up supervised learning more efficient.⁴⁵ Second Generation Machine Learning includes deep learning and surpasses First Generation Machine Learning because it is limited in its accuracy by relying on programmed rules.⁴⁶ In contrast, deep learning algorithms allow machines to receive data and self-develop complex functions to provide predictions.⁴⁷

Predictive algorithms have already been put into practice in the diagnosis, prevention, and treatment of cancer.⁴⁸ IBM's Watson for Oncology best exemplifies this case.⁴⁹ Watson is the first system to fully understand questions posed in natural language and to tap into the entire body of medical knowledge and the personal records of a patient to develop a diagnosis or treatment plan in less than three seconds.⁵⁰ Watson also supplements the surfaced treatment options with relevant evidence from the literature by leveraging natural language processing and advanced machine learning algorithms to search a corpus of over 300 medical journals, 250 textbooks, and 15 million pages of text.⁵¹ In Japan, Watson saved a sixty-year-old woman by identifying her rare form of leukemia and took just about ten minutes to compare the patient's genetic changes with a database of twenty million cancer research papers.⁵² However, Watson has not reached the stage of deep learning, because the information on how patients with specific characteristics should be treated is determined by human overseers.⁵³ Watson is also not fault-proof, as recent studies show it making wrong and unsafe treatment recom-

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45. Fei Jiang et al., *Artificial Intelligence in Healthcare: Past, Present and Future*, 2 *STROKE & VASCULAR NEUROLOGY* 230, 234 (2017).
 46. Fogel & Kvedar, *supra* note 3, at 1.
 47. *Id.*
 48. See Ricvan Dana Nindrea et al., *Diagnostic Accuracy of Different Machine Learning Algorithms for Breast Cancer Risk Calculation: A Meta-Analysis*, 19 *ASIAN PAC. J. CANCER PREVENTION* 1747 (2018).
 49. *IBM Watson for Oncology*, IBM, <https://www.ibm.com/us-en/marketplace/ibm-watson-for-oncology/details> (last visited Aug. 26, 2019).
 50. Jessica S. Allain, *From Jeopardy! to Jaundice: The Medical Liability Implications of Dr. Watson and Other Artificial Intelligence Systems*, 73 *LA. L. REV.* 1049, 1050–51 (2013).
 51. *IBM Watson for Oncology*, *supra* note 49.
 52. Jon Fingas, *IBM's Watson AI Saved a Woman from Leukemia*, *ENGADGET* (Aug. 7, 2016), <https://www.engadget.com/2016/08/07/ibms-watson-ai-saved-a-woman-from-leukemia/>.
 53. Casey Ross & Ike Swetlitz, *IBM Pitched Its Watson Supercomputer as a Revolution in Cancer Care. It's Nowhere Close*, *STAT* (Sept. 5, 2017), <https://www.statnews.com/2017/09/05/watson-ibm-cancer/>.

mendations in some cases.⁵⁴ Despite its current downsides, Watson provides us with an insight of what predictive algorithm is capable of achieving.

III. PATENT ELIGIBILITY INQUIRY FOR ALGORITHM

A. Algorithm Demystified

1. What is an Algorithm?

In order to assess the patent eligibility for predictive algorithms, it is instructive to understand what an algorithm is. In general, an algorithm is a set of instructions for solving a problem.⁵⁵ For some, an algorithm is an abstract idea because it is a series of instructions, written in a high-level form of expression, that can be carried out by a generic machine. It is a law of nature, a mathematical idea, or an idea, and, until the specific device is specified, an algorithm cannot be constructed.⁵⁶ However, it is important to note that an algorithm can be expressed in different ways, using divergent expressions at different levels of sophistication and abstraction.⁵⁷ An algorithm is not necessarily dependent on computers⁵⁸ or devised to solve problems of a mathematical nature.⁵⁹ In fact, every computer program is an algorithm because for computers to perform any useful task they need to be told what to do.⁶⁰ These instructions make up the algorithm called the program, and this uses a number of algorithms to produce a certain result.⁶¹ The function of the program is its purpose, as distinguished from how it accomplishes that purpose (the algorithm) or what is produced (the output).⁶²

54. Meg Bryant, *STAT: IBM's Watson Gave 'Unsafe and Incorrect' Cancer Treatment Advice*, HEALTHCARE DIVE (July 26, 2018), <https://www.healthcarediver.com/news/stat-ibms-watson-gave-unsafe-and-incorrect-cancer-treatment-advice/528666/>.

55. Allen C. Zoracki, *When is an Algorithm Invented? The Need for A New Paradigm for Evaluating an Algorithm for Intellectual Property Protection*, 15 L.J. SCI & TECH. 579, 581 (2005).

56. Mitchell P. Novick & Helene Wallenstein, *Algorithm and Software Patentability*, 7 RUTGERS COMP. & TECH. L.J. 313, 335 (1980).

57. John Swinson, *Copyright or Patent or Both: An Algorithmic Approach to Computer Software Protection*, 5 HARVARD J.L. & TECH. 145, 145 (1991).

58. *Id.* at 146–47.

59. Niklaus Wirth, *Data Structures and Algorithms*, 251 SCI. AM. 60, 65 (Sept. 1984).

60. Swinson, *supra* note 57, at 147.

61. *Id.* at 147–48.

62. *Id.* at 149.

An algorithm, therefore, is not a natural phenomenon or abstract concept, because one cannot conceive an algorithm in nature.⁶³ An algorithm does not describe a natural phenomenon.⁶⁴ In fact, it does not describe anything other than a series of operations to be performed by a machine or human being. Hence, algorithms are highly specific rather than abstract.⁶⁵ The Federal Circuit also shared this view: “. . . a mathematical algorithm does not appear in nature at all, but only in human numerical processes. . . . It is difficult to determine how or why mathematical algorithms are ‘like’ laws of nature.”⁶⁶ In summary, Swinson has explained that an algorithm can be understood as having the following features: (1) having a set of instructions that are followed by a processor to carry out a process, which need not have anything to do with mathematics; (2) not dependent on having a digital computer as the processor; (3) every computer program is the expression of at least one algorithm; and (4) can be used to solve many problems, not just mathematical problems.⁶⁷

B. Algorithm Patent Eligibility: The View from the U.S. Supreme Court

1. In the 20th Century

Under 35 U.S.C. § 101 (Section 101), patents can be granted for machines, manufactures, processes or compositions of matter.⁶⁸ An invention has to fall into one of these four categories in order to be patent eligible.⁶⁹ Although the patent eligible category is rather broad under Section 101, the Supreme Court has created three judicial exceptions which are not patentable:⁷⁰ “laws of nature, natural phenomenon and abstract ideas.”⁷¹ In the 20th

63. Donald S. Chisum, *The Patentability of Algorithms*, 47 *UNIV. PITT. L. REV.* 959, 980 (1986).

64. *Id.* at 980–81.

65. *Id.* at 981.

66. *Arrhythmia Research Tech. v. Corazonix Corp.* 958 F.2d 1053, 1066 (Fed. Cir. 1992).

67. Swinson, *supra* note 57, at 150.

68. 35 U.S.C. § 101 (2012).

69. *Id.*

70. *Alice Corp. Pty. v. CLS Bank Int’l*, 573 U.S. 208, 216 (2014) (quoting *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.* 569 U.S. 576, 579 (2013)).

71. *Le Roy v. Tatham*, 55 U.S. 156, 175 (1852) (Abstract ideas have been defined as “[a] principle, in the abstract, is a fundamental truth; an original cause; a motive; these cannot be patented, as no one can claim in either them an exclusive right.”).

Century, the Supreme Court was doubtful with the patent eligibility of an algorithm in the beginning but gradually accepted it under different tests.⁷²

First, under *Gottschalk v. Benson*, pure algorithms are unpatentable as abstract ideas.⁷³ Prior to *Benson*, there was no patent law definition for an algorithm, which the court has defined as “a procedure for solving a given type of mathematical problem.”⁷⁴ Second, in *Parker v. Flook*, the Court found that simply limiting an abstract idea to a particular application or adding post-solution activity is insufficient to overcome the threshold of patentable subject matter.⁷⁵ In order to be patent eligible, the algorithm needs to present an “inventive concept.”⁷⁶ Lastly, in *Diamond v. Diehr*, the Supreme Court held that a computer program is not automatically an “abstract idea” or “algorithm” that precluded patent protection.⁷⁷ Considering the patent claims as a whole, the Court held that, although the method only provided application of laws of nature and mathematical formulas, a known process is patent eligible when the method provides a sufficient way to transform a particular article into a different state or thing.⁷⁸ The holding in *Diehr* solidified *Flook*’s Machine-or-Transformation test, which states that a method is patentable only if: (1) the method is tied to a particular machine; or (2) the method transforms a particular article into a different state or thing.⁷⁹

2. In the 21st Century

In the 21st Century, just when *Diehr* was decided, another three cases called the assumption that algorithms could be patent eligible into question. The first case was *Bilski v. Happos*, which involved a method for predicting the risk of a commodity trade in the energy market using shadow transactions.⁸⁰ The Supreme Court held that the Machine-or-Transformation test is not dispositive in determining eligibility of process under Section 101; it is only a “useful and important clue.”⁸¹

72. *Parker v. Flook*, 437 U.S. 584, 585, 590–91 (1978).

73. *Gottschalk v. Benson*, 409 U.S. 64, 71–4 (1972).

74. *Chisum*, *supra* note 63, at 974.

75. *Flook*, 437 U.S. at 590, 594.

76. *Id.* at 594 (“Even though a phenomenon of nature or mathematical formula may be well known, an inventive application of the principle may be patented. Conversely, the discovery of such a phenomenon cannot support a patent unless there is some other inventive concept in its application”).

77. *Diamond v. Diehr*, 450 U.S. 175, 184–89 (1981).

78. *Id.* at 191–92.

79. *Id.*

80. *Bilski v. Happos*, 561 U.S. 593, 599 (2010).

81. *Id.* at 603.

The second case, *Mayo v. Prometheus*, extended this prohibition to medical diagnostic algorithms, which the court considered as laws of nature.⁸² The claim concerned a typical First Generation Personalized Medicine process involving three steps in the administering doses of the thiopurine drugs based on one-to-one correlation measuring dosage level according to a known biomarker.⁸³ The claim tells the doctors to: (1) measure the current level of the relevant metabolite; (2) use particular laws of nature to calculate the current toxicity/inefficacy limits; and (3) reconsider the drug dosage in light of the law. The *Mayo* Court considered the steps simply as instructions that add nothing specific to the laws of nature (dosage/metabolite correlation) other than routine, conventional activity.⁸⁴ The significant part of *Mayo* was the establishment of a two-step test for assessing patent eligibility.⁸⁵ First, determine if the invention is directed to one of the judicial categories of ineligible subject matter.⁸⁶ If so, second, ask whether the patent claims add enough to their statement of the correlations of laws of nature to allow the processes they describe to qualify as patent-eligible process that apply natural laws.⁸⁷

Recently, in *Alice Corp. Pty. v. CLS Bank International*, the Supreme Court reaffirmed *Mayo*'s two part test and applied it to claims directed to a computerized process to mitigate settlement risk.⁸⁸ The claims in *Alice* dealt exclusively with utilizing the method, a computer system to carry out the method, and software for performing the method.⁸⁹ In *Alice*, the patent claims involve: (1) the foregoing method for exchanging obligations (the method claim); (2) a computer system configured to carry out the method for exchanging obligations (the systems claim); and (3) a computer readable medium containing program code for performing the method of exchanging obligations (the media claim), all of which required the use of computer.⁹⁰ The Supreme Court asserted that certain claims involving computer software constituted ineligible subject matter under Section 101 of the Patent Act.⁹¹ Using step one of the *Mayo* test, the Court found that *Alice*'s intermediated settlement is an abstract idea, and by merely requiring a generic computer to

82. *Mayo Collaborative Servs. v. Prometheus Labs.*, 566 U.S. 66, 91–92 (2012).

83. *Id.* at 82.

84. *Id.*

85. *Id.* at 77.

86. *Id.*

87. *Id.*

88. *Alice Corp. Pty. v. CLS Bank Int'l*, 573 U.S. 208, 217–18 (2014).

89. *Id.* at 214.

90. *Id.*

91. *Id.* at 212.

implement, it failed to transform that abstract idea into a patent-eligible invention under step two of the *Mayo* test.⁹²

IV. PATENT ELIGIBILITY FOR PREDICTIVE ALGORITHM POST *MAYO* AND *ALICE*

A. The Death of Method Patents?

Following *Alice*, *Ariosa Diagnostics v. Sequenom* addressed another typical First Generation Personalized Medicine process invention, and the Federal Circuit affirmed the invalidation of the patent using the *Mayo-Alice* test.⁹³ The patent in question was directed to certain methods of using cell-free fetal DNA (cffDNA). The inventors discovered cffDNA in maternal plasma and serum, the portion of maternal blood samples that other researchers had previously discarded as medical waste.⁹⁴ By applying a combination of known laboratory techniques to their discovery, the inventors implemented a method for detecting the small fraction of paternally inherited cffDNA in maternal plasma or serum to determine fetal characteristics, such as gender.⁹⁵

The invention, commercialized by Sequenom as its MaterniT21 test, created an alternative for prenatal diagnosis of fetal DNA that avoids the risks of widely-used techniques that took samples from the fetus or placenta.⁹⁶ The patent did not claim cffDNA itself, but rather the method of using it. The steps include: (1) extracting DNA from the serum or plasma samples; (2) amplifying by polymerase chain reaction (PCR) or another method; (3) detecting, in which the lab technician adds the amplified cffDNA to an agarose gel containing ethidium bromide to stain and visualize the paternally inherited cffDNA; and (4) diagnosing certain fetal characteristics based on the detection of paternally inherited cffDNA.⁹⁷

By using the *Mayo-Alice* test, the Federal Circuit found that the patent was directed to a multistep method, starting with cffDNA taken from a sample of maternal plasma or serum—a naturally occurring non-cellular fetal DNA that circulates freely in the blood stream of a pregnant woman.⁹⁸ The inventors have not created or altered any of the genetic information encoded in the cffDNA, and it is undisputed that the location of the nucleic acids existed in nature before the inventors found them.⁹⁹ The court held that the

92. *Id.*

93. *Ariosa Diagnostics v. Sequenom*, 788 F.3d 1371, 1375 (Fed. Cir. 2015).

94. *Id.* at 1376.

95. *Id.*

96. *Id.* at 1381.

97. *Id.* at 1373–74.

98. *Id.* at 1376.

99. *Ariosa Diagnostics*, 788 F.3d at 1376.

method therefore begins and ends with a natural phenomenon, so the claims are directed to a matter that is naturally occurring, hence falling in the Step 1 of the *Mayo-Alice* test.¹⁰⁰

Under Step 2 of the *Mayo-Alice* test, the Federal Circuit found that all the steps are general instructions for doctors to apply routine, conventional techniques when seeking to detect cffDNA.¹⁰¹ Because method steps were well-understood, conventional, and routine, the method of detecting paternally inherited cffDNA is not new and useful.¹⁰² The only new and useful subject matter as of the date of the application was the discovery of the presence of cffDNA in maternal plasma or serum, hence Seprenom also failed Step 2 of the test.¹⁰³ By rejecting the patent eligibility of this invention, some commentators fear that *Alice* is a prelude to the death of method patents¹⁰⁴ or the rejection of all software patents.¹⁰⁵

B. Implication of *Mayo-Alice* on Predictive Algorithm

Will the *Mayo-Alice* test hinder the development of Second Generation Personalized Medicine, especially predictive algorithms? Using IBM's Watson as an example, a hypothetical patent application could include the following claims: (1) a Collecting step: collect the medical Big Data of the patient (such as -omics data, electronic medical record, family history, notes from previous office visits and test result); (2) an Application step: use predictive algorithm to find the pattern and correlation in data, analysis the data; summaries and highlights futures of particular significance; (3) an Additional step: the algorithm lists several additional options for physician to input (e.g. comorbidities and disease status); and (4) a Resulting step: provide physicians with diagnosis or treatment recommendations for specific patients supported with evidence. Lastly, the physician could take recommendations into consideration when choosing to adopt or reject it. The major difference between First Generation Personalized Medicine and Second Generation Medicine is in stage two, where sophisticated predictive algorithms are able to find correlation, patterns between medical Big Data and the patient, and this process could be incomprehensible or incapable by humans alone.¹⁰⁶

100. *Id.*

101. *Id.* at 1377.

102. *Id.*

103. *Id.* at 1377.

104. Timothy J. Busse, *The Relativity of an Abstract Idea: A Practicable Approach to Alice's Inventive Concept*, HOUST. BUS. & TAX L.J. 252, 255 (2016).

105. Gene Quinn, *SCOTUS Rules Alice Software Claims Patent Ineligible*, IPWATCHDOG (June 19, 2014), <http://www.ipwatchdog.com/2014/06/19/scotus-rules-alice-software-claims-patent-ineigible>.

106. See Ross & Swetlitz, *supra* note 53 (Doctors in South Korea pointed out an issue regarding Watson that it provides recommendations and supporting evi-

Unlike First Generation Personalized Medicine, with clear and well understood correlations, the algorithm could result in correlations that are undiscovered. In addition, the process on how the algorithm reached its conclusion could often be opaque or unexplainable.¹⁰⁷ Despite the complexity, will the court still find the result merely an undiscovered law of nature as in step 1 of the *Mayo-Alice* test? If so, the second step of the *Mayo-Alice* test asks the court to examine the elements of the claim to determine whether it contains an “inventive concept” sufficient to “transform” the claimed abstract idea into a patent eligible application.¹⁰⁸ A claim that is directed to an abstract idea must have “additional features” to prevent the monopolization of patent ineligible subject matter.¹⁰⁹ Some of the features in predictive algorithms fall right within the limitations specifically pointed out by the Supreme Court. For example, the claim must do more than instruct one to apply the applicable laws.¹¹⁰ Also, a computer implementation does not supply the necessary inventive concept.¹¹¹ Finally, merging it together and applying it using a computer results in the same deficient outcome.¹¹²

Post *Mayo* and *Alice*, one might infer that claims directed to software-related inventions are now required to show a technical improvement or an improvement to the functioning of the computer running the software.¹¹³ The United States Patent and Trademark Office (USPTO) has also issued a memorandum providing examples of what constitutes “significantly more” improvement, such as improvements to another technology or technical field, improvements to the functioning of the computer itself, and meaningful limitations beyond generally linking the use of an abstract idea to a particular technological environment.¹¹⁴ Commentators have argued that after *Mayo* and *Alice*, patenting pure algorithms requires significantly more than just the

dences but does not really tell the physician how it came up with the particular treatment recommendation for particular patient).

107. See, e.g., Turgay Ayer et al., *Breast Cancer Risk Estimation with Artificial Neural Networks Revisited: Discrimination and Calibration*, 116 *CANCER* 3310, 3318 (2010).

108. *Alice Corp. Pty. v. CLS Bank Int’l*, 573 U.S. 208, 221 (2014).

109. *Id.*

110. *Id.*

111. *Id.* at 222.

112. See *id.* (“simply implementing a mathematical principle of a physical machine, namely a computer, is not a patentable application of that principle”).

113. Natalya Dvorson & Mark C. Davis, *Through the Looking Glass: Exploring the Wonderland of Patent Subject Matter Eligibility after Alice Corp. v. CLS Bank International*, 7 *LANDSLIDE* 8, 10 (2014).

114. U.S. PATENT & TRADEMARK OFFICE, PRELIMINARY EXAMINATION INSTRUCTIONS IN VIEW OF THE SUPREME COURT DECISION IN *Alice Corporation Pty. LTD. v. CLS BANK INTERNATIONAL, ET AL.* (June 25, 2014), https://www.uspto.gov/sites/default/files/patents/announce/alice_pec_25jun2014.pdf.

algorithm itself, which will either be held a product of nature or an abstract idea.¹¹⁵ Some commentators suggest the easiest way to overcome this patenting obstacle is to add “something more,” such as diagnostics.¹¹⁶ This leads innovators to turn away from developing complex algorithms and instead focus on a simpler, more explicit relationship that can be tied to a physical product or process.¹¹⁷

C. *Mayo* and *Alice*: Underlying Confusion

Looking closely at *Mayo* and *Alice*, one comes across several keywords such as “purely conventional,” “inventive concept,” and “significantly more” that the Supreme Court used to reject patent eligibility.¹¹⁸ These terms, however, are very similar to the terms used in judging obviousness in Section 103.¹¹⁹ Furthermore, the Supreme Court has been emphasizing the danger of “pre-emption” that patents will not be granted to preempt the basic building blocks of human ingenuity.¹²⁰ By stressing on the inventor’s actual contribution to the field, the Supreme Court is looking into the breadth of claims under the realm of Section 112, using written description and enablement.¹²¹ *Mayo* and *Alice* hence create: (1) confusing policies underlying patent eligi-

115. Price, *Black Box Medicine*, *supra* note 16, at 445.

116. *Id.*

117. *Id.*

118. *See Mayo Collaborative Servs. v. Prometheus Labs.*, 566 U.S. 66, 79 (2012); *see also Alice Corp. Pty. v. CLS Bank Int’l*, 573 U.S. 208, 215–17 (2014).

119. 35 U.S.C. § 103 (2012) (“A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made”).

120. *See Alice*, 573 U.S. at 216–17 (“We have described the concern that drives this exclusionary principle as one of preemption. . . . Those that integrates the building blocks into something more . . . pose no comparable risk of pre-emption, and therefore remain eligible of the monopoly granted under our patent laws”).

121. 35 U.S.C. § 112(a)–(b) (2012) (“The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art . . . to make and use the same. . . . The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor . . . regards as the invention”).

bility as compared to other patent law doctrines; and (2) a confusing test governing patent eligibility.¹²²

By using patent eligibility to assess obviousness of an invention, the court has caused confusion in applying Sections 101 and 103.¹²³ Because the components of a claim may not be assessed individually under Section 103, claims are analyzed individually and as a whole when determining if the additional elements of a patent transform the abstract idea into a patent eligible matter under Section 101.¹²⁴ By allowing a claimed invention to be dissected into its individual components, the Supreme Court is allowing Section 101 to do what is not an option under Section 103: looking at the individual claims of an invention for obviousness.¹²⁵ Justice Stewart warns against the majority's use of "inventive application" in his dissent in *Flook*.¹²⁶

Further, questions include the difference between the inventive concept required in Sections 101 and 103: while obviousness is judged from the view of a person having ordinary skill in the art, would this person also be used to judge inventive concept in Section 101? This ambiguous and heightened bar for patent eligibility has led lower courts to refuse patents.¹²⁷ Rejecting predictive algorithm claims during the subject matter inquiry and looking into the claims separately at the subject matter eligibility stage saves the court the peril of hindsight bias when assessing obviousness. However, by fusing the subject eligibility and obviousness requirement, the U.S. approach might reject many potentially patentable inventions prematurely.

V. PREDICTIVE ALGORITHM PATENT ELIGIBILITY UNDER THE EPO APPROACH

Some commentators, however, have found that the Supreme Court's confusing test might be reasonable because, surprisingly, the Supreme Court's construction of patentable subject matter seems to reach a similar

122. David O. Taylor, *Confusing Patent Eligibility*, 84 TENN. L. REV. 157, 186 (2016).

123. Paxton M. Lewis, *The Conflation of Patent Eligibility and Obviousness: Alice's Substitutions of Section 103*, UTAH L. REV. ON LAW 13, 28 (2017).

124. *Id.*

125. *Id.* at 30.

126. *Parker v. Flook*, 437 U.S. 584, 600 (1978) ("It strikes what seems to me an equally damaging blow at basic principles of patent law by importing into its inquiry under 35 U.S.C. section 101 the criteria of novelty and inventiveness. Section 101 is concerned only with subject matter patentability. Whether a patent will actually issue depends upon the criteria of section 102 and section 103").

127. Taylor, *supra* note 122, at 237.

result as the European Patent Office (EPO).¹²⁸ By applying the “inventive concept” test during the second step of Section 101’s subject matter determination, not only could the Supreme Court avoid the hindsight bias prohibition under Section 103, but it could also provide a similar standard on the subject matter jurisprudence on both sides of the Atlantic.¹²⁹

Could it be possible that the Supreme Court is aiming for a higher purpose, the global harmonization of patent law, rather than creating a bright line rule for patentable subject matter inquiry? Even if this is the case, should the Supreme Court take this matter in hand or should the Court leave it for Congress to decide? The more important question is: has the *Mayo-Alice* test actually reached the result similar to the European approach?

A. What Constitutes Patent Eligible Subject Matter?

In Europe, Article 52 of the European Patent Convention (EPC) states that patents shall be granted for any inventions in all fields of technology, provided that they are new, involve an inventive step, and are susceptible of industrial application.¹³⁰ Specifically, EPC Article 52(2) (a–d) suggests that: (1) Discoveries; (2) Scientific theories; (3) Mathematical methods; (4) Aesthetic creations; (5) Schemes; (6) Rules and methods for performing mental acts; (7) Playing games or doing business; (8) Programs for computers; and (9) Presentations of information might not be considered as invention under EPC 52(1), but they are only prohibited “as such.”¹³¹ By providing evidence of some technical effects, they will be patent eligible.¹³²

Unlike the United States, where an invention has to fall under one of the Section 101 categories, EPO requires the invention be of “technical character” to the extent that it must relate to a technical field,¹³³ must be concerned with a technical problem,¹³⁴ and must have technical features in terms of the matter for which protection is sought and can be defined in the claim.¹³⁵ In regard to software related inventions, whether algorithms are patent eligible was also an issue for EPO.¹³⁶ Throughout the years, EPO’s Technical Boards

128. Dan L. Burk, *The Inventive Concept in Alice Corp. v. CLS Bank Int’l*, 46 INT’L REV. INTELL. PROP. & COMPETITION 865 (2014).

129. *Id.* at 867.

130. Eur. Pat. Convention Article 52(1) (2016) [hereinafter EPC].

131. EPC Article 52(2).

132. *See, e.g., Guidelines for Examination in the EPO*, Part G – Chapter II-2 (2017); *see also e.g., Euro. Pat. Off. Tech. Ct. App. T0258/03*, Apr. 21, 2004 (“Activities falling within the notion of a non-invention ‘as such’ would typically represent purely abstract concepts devoid of any technical implications.”).

133. EPC Rule 42(1)(a).

134. EPC Rule 43(1).

135. *Id.*

136. *See Guidelines for Examination in the EPO*, Part G – Chapter II-3.6 (2017).

of Appeal (TBA) has deployed different tests through various cases. For example, in T208/84,¹³⁷ “technical contribution approach”¹³⁸ was introduced. In T1173/97,¹³⁹ TBA adopted the “technical effect approach”¹⁴⁰ which, for the first time, allows the patent eligibility of computer program. Finally, in T258/03,¹⁴¹ the EPO settled on the “any apparatus” approach.¹⁴² Under this approach, as long as the claims of a patent recite some apparatus, the claim will meet the Article 52 requirement.¹⁴³ In light of the case law of the TBA, an invention is to be construed as “subject matter having technical matter.”

B. T258/03 *Hitachi and Alice*

Before assessing the patent eligibility for Second Generation Personalized Medicine predictive algorithms in Europe, it might be instructive to look at a TBA decision to see the similarities and differences between the EPO and U.S. approach. In T258/03 *Hitachi*, the main request for the patent in-

137. Euro. Pat. Off. Tech. Ct. App. T208/84, July 15, 1987.

138. *Id.* at 19 (“Decisive is what technical contribution the invention as defined in the claim when considered as whole makes the known art”).

139. Euro. Pat. Off. Tech. Ct. App. T1173/97, July 1, 1998.

140. *Id.* at 620–21 (“[C]ould be found in the further technical effects deriving from the execution (by the hardware) of the instructions given by the computer program . . . where they cause the software to solve a technical problem, an invention which brings about such an effect may be considered an invention . . . Consequently a patent may be granted . . . in every case where a program for a computer is the only means, or one of the necessary means, of obtaining a technical effect within the meaning specified above, where, for instance, a technical effect of the kind is achieved by the internal functioning of a computer itself under the influence of said program”).

141. Euro. Pat. Off. Tech. Ct. App. T258/03.

142. *Id.* at 585 (“What matters having regard to the concept of invention within the meaning of Article 52(1) EPC is the presence of technical character, which may be implied by the physical features of an entity or the nature of an activity, or may be conferred to non-technical activity by the use of technical means. In particular, the Board holds that the latter cannot be considered to be non-invention ‘as such’ within the meaning of Article 52 (2) and (3) EPC. Hence, in the Board’s view, activities falling within the notion of a non-invention “as such” would typically represent purely abstract concepts devoid of any technical implication. The Board is aware that its comparatively broad interpretation of the term ‘invention’ in Article 52 (1) EPC will include activities which are so familiar that their technical character tends to be overlooked, such as the act of writing using pen and paper It is therefore concluded that, in general, a method involving technical means is an invention within the meaning of Article 52(1) EPC”).

143. Euro. Pat. Off. Tech. Ct. App. T 2258/10, Oct. 4, 2011 (“Following T 931/95 (OJ EPO 2001, 441), see headnote III, any apparatus constituting a physical entity or concrete product has technical character”).

cludes: claim one, “automatic auction method executed in a server computer”; claim two, a “computerized auction apparatus’s comprising a server computer is defined,” and claim three, “a computer for carrying out an auction.” In simple terms, the claims are similar to *Alice*: first an abstract idea, auction, and second, merely reciting a generic computer.¹⁴⁴

However, unlike *Alice*, TBA first acknowledged earlier decisions, saying that any comparison with the prior art was inappropriate because determining the technical contribution of an invention involves assessing the prior art, which is more appropriate during examination of novelty and inventive step.¹⁴⁵ TBA then states that because it is difficult to separate a claim into technical and non-technical features, finding a technical aspect should be done when assessing inventive step.¹⁴⁶ TBA further states that only purely abstract concepts will be devoid of any technical implications.¹⁴⁷ As long as there is presence of technical character, which might be implied by the physical features of an entity or the nature of an activity, or may be conferred to non-technical activity by the use of technical means (e.g. a computer), then that will satisfy the concept of invention in Article 52(1).¹⁴⁸

Although the *Hatchi* invention satisfied Article 52(1) of the EPC for patent eligibility, it nonetheless failed the inventive step requirement in Article 56 of the EPC.¹⁴⁹ The reason is that the invention involves a feature for when more than one bidder offers a certain “desired price,” the auction price is increased to sort out the lower bids.¹⁵⁰ This requires certain bid information—“a desired price” and a “maximum price.”¹⁵¹ However, the feature is fundamentally independent of the computer arrangement for performing the auction.¹⁵² One could just conduct a Dutch auction without computer support and instead collect bids in writing in a call for tender in order for the participants not to be present at the auction.¹⁵³ Therefore, TBA reasoned that the

144. Euro. Pat. Off. Tech. Ct. App. T258/03, pp. 2–4, Apr. 21, 2004.

145. Euro. Pat. Off. Tech. Ct. App. T1173/97, p. 17, July 1, 1998.

146. Euro. Pat. Off. Tech. Ct. App. T258/03, p. 5.

147. *Id.* at p. 6.

148. *Id.*

149. EPC Article 56 (2016) (“an invention shall be considered as involving an inventive step if, having regard to the state of the art, it is not obvious to a person skilled in the art. If the state of the art also includes documents within the meaning of Article 54, paragraph 3, these documents shall not be considered in deciding whether there has been an inventive step”).

150. Euro. Pat. Off. Tech. Ct. App. T258/03, p. 4.

151. *Id.*

152. *Id.* at 7.

153. *Id.*

invention could be regarded as a mere automation of a non-technical activity of performing a Dutch auction.¹⁵⁴

Unlike the U.S. approach, the EPO did not bar the patent eligibility of the invention because, although it claims an abstract idea, a Dutch auction is deemed to have a technical feature by reciting a computer in the claims.¹⁵⁵ However, this invention failed to satisfy the inventive step of the patentability test because the steps do not necessarily need a computer to accomplish the task.¹⁵⁶ The result might have been different, however, if a step had been designed in such a way as to be particularly suitable for being performed on a computer, because then it would arguably have had a technical character to satisfy the inventive step.¹⁵⁷

C. Similar Results between the United States and EPO?

For a Second Generation Personalized Medicine predictive algorithm to be considered an invention in Europe, it needs to possess technical character.¹⁵⁸ According to T38/86, headnote III, the use of technical means that carrying out a method for performing mental acts, partly or entirely without human intervention, may, under Article 52(3) of the EPC, render such a method a technical processes or method, and, therefore, an invention within the meaning of Article 52(1) of the EPC.¹⁵⁹ This applies even if the technical means are commonly known. For example, the inclusion of a computer, a computer network, a readable medium carrying a program, etc. in a claim

154. *Id.*

155. *Id.* at 6.

156. Euro. Pat. Off. Tech. Ct. App. T258/03, p. 4.

157. Euro. Pat. Off. Tech. Ct. App. T0769/92, p. 2, May 31, 1994. (“General purpose management system (1994), headnote 1 (An invention comprising functional features implemented by software (computer programs) is not excluded from patentability under Article 52(2)(c) and (3) EPC if technical considerations concerning particulars of the solution of the problem the invention solves are required in order to carry out that same invention. Such technical considerations lend a technical nature to the invention in that they imply a technical problem to be solved by (implicit) technical features”).

158. *Guidelines for Examination in the European Patent Office*, Part G(II)(3.6) (2017).

159. Euro. Pat. Off. Ct. Tech. App. T 0038/86, p. 2, Feb. 14, 1989.

lends technical character to the claimed subject matter.¹⁶⁰ Hence, the EPO sets a low threshold for showing evidence of technical effects.¹⁶¹

Following the EPO's approach, a Second Generation Personalized Medicine predictive algorithm would be considered an invention and patent eligible, despite the fact that it might show correlations that point toward abstract ideas (such as the hypothetical correlation step 2 *supra*), because data collection in step one will not be seen as merely routine or conventional since prior arts are not to be compared during the patent eligibility stage.¹⁶² The reciting of computer in the claim further enhances the technicality of the invention. The potential opacity of the collection, step two, illustrates that this process is beyond human comprehension and particularly suitable to being performed on a computer so as to satisfy the inventive step as suggested in T 769/92, headnote one.¹⁶³

By assessing both *Alice-Mayo* and the EPO test on a software-related invention, the result is diverse. Unlike what some commentators have suggested, the result across the Atlantic does not have a similar standard on subject matter inquiry.¹⁶⁴ In the United States, the courts can view the claims as a whole and separately to determine subject matter eligibility when looking at the inventions as a whole and assessing for obviousness.¹⁶⁵ In Europe, the claims are viewed as a whole in assessing whether the claimed subject matter is an invention and separately and as a whole in the assessment for the inventive step.¹⁶⁶ By going opposite directions, under *Alice-Mayo*, a predica-

160. *Guidelines for Examination in the European Patent Office*, G(II)(3.6) (2017) (This section of Guidelines for Examination provides some examples regarding technical effects on software-related inventions, such as: "A further technical effect which lends technical character to a computer program may be found e.g. in the control of an industrial process or in the internal functioning of the computer itself or its interfaces under the influence of the program and could, for example, affect the efficiency or security of a process, the management of computer resources required or the rate of data transfer in a communication link").

161. *Id.*

162. *Id.*

163. Euro. Pat. Off. Tech. Ct. App. T 0769/92, p. 2.

164. Siva Thambisetty, *Alice and 'Something More': The Drift Towards European Patent Jurisprudence*, 3 J. L. & BIOSCIENCES 691, 694 (2016).

165. *See generally* *Alice Corp. Pty. v. CLS Bank Int'l*, 134 S. Ct. 2347 (2014).

166. *Guidelines for Examination in the European Patent Office*, Part G (VII)(6) (2017), ("When assessing the inventive step of such a mixed-type invention, all those features which contribute to the technical character of the invention are taken into account However, features which do not contribute to the technical character of the invention cannot support the presence of an inventive step").

tive algorithm might be rejected prematurely at the subject matter phase.¹⁶⁷ On the other hand, it is relatively easy to become an invention in Europe.¹⁶⁸ Put simply, Europe is currently more patent friendly than the United States in the field of software-related inventions.¹⁶⁹

VI. PATENT POLICY RECOMMENDATION FOR PREDICTIVE ALGORITHM IN THE UNITED STATES

A. *Mayo-Alice* Failed to Foster Innovation

The role of patents, as stated in the U.S. Constitution, is to promote the progress of arts and sciences.¹⁷⁰ For a long time, the United States has been heralded as the world leader in prompting technological innovation.¹⁷¹ However, this position is now questionable as the U.S. patent system is increasingly mired in legal uncertainty.¹⁷² According to Sachs, in the three years following the Supreme Court's last Section 101 decision in *Alice*, there have been 473 Federal Circuit and district court Section 101 decisions, 317 of which invalidated the patents at issue in whole or in part.¹⁷³ Of these 473 cases, 60% of all challenged patents were found to be invalid, while 66.4% of all claims were invalidated.¹⁷⁴ The Federal Circuit informs us by number just how much impact *Alice* brings to inventors, with 80 of 88 patents having been invalidated.¹⁷⁵

This creates a serious concern because algorithms are becoming increasingly important in today's economy.¹⁷⁶ Gartner has predicted that by 2019, 250,000 patent applications will include claims for algorithms, a tenfold in-

167. Michael Borella, *The Subject Matter Eligibility of Machine Learning: An Early Take*, PATENT DOCS (Sept. 23, 2018), <https://www.patentdocs.org/2018/09/the-subject-matter-eligibility-of-machine-learning-an-early-take.html>.

168. Jim Ruttler, *EPO v. USPTO Examination*, RULLER MILLS PLLC (Apr. 24, 2016), <http://ruttlermills.com/Blog/EPO-vs.%20USPTO%20Examination>.

169. Dennis Crouch, *Patenting Software in the US as Compared with Europe*, PATENTLYO (Sept. 29, 2014), <https://patentlyo.com/patent/2014/09/patenting-software-compared.html>.

170. See U.S. CONST. art 1, § 8, cl.8.

171. Kevin Madigan & Adam Mossoff, *Turning Gold into Lead: How Patent Eligibility Doctrine is Undermining U.S. Leadership in Innovation*, 24 GEO. MASON L. REV. 939 (2017).

172. *Id.* at 24.

173. Robert Sachs, *Alicestorm Update for Q1 2017*, BILSKIBLOG (Apr. 6, 2017), <http://www.bilskiblog.com/blog/2017/04/alicestorm-update-for-q1-2017.html>.

174. *Id.*

175. *Id.*

176. Michael Cooney, *Gartner: Algorithm-Based Technology Patents are Raging*, NETWORKWORLD (Feb. 8, 2017), <https://www.networkworld.com/article/3167242/security/gartner-algorithm-based-technology-patents-are-raging.html>.

crease from five years ago.¹⁷⁷ By labeling the next wave of economy as the algorithm economy, which helps to power the machine-to-machine evolution in the Internet of Things, the algorithm is where the real value lies by turning data into actions.¹⁷⁸ However, of the top forty organizations patenting the most algorithms in the past five years, thirty-three are Chinese businesses and universities, while the only western company in the top ten is IBM at number ten.¹⁷⁹ It is not surprising that commentators have warned that the gold standard of the U.S. patent system is eroding while Europe and China are catching up.¹⁸⁰

1. *Mayo-Alice*: The Way Forward?

Many commentators have expressed concerns with the Court's decision in *Alice* and proposed amendments to Section 101, even proposing to abolish Section 101 altogether.¹⁸¹ The American Intellectual Property Law Association (AIPLA) has proposed legislative amendments to Section 101 relating to patent eligibility.¹⁸² Michelle Lee, the former Director of USPTO, has also acknowledged that changes may need to be made to Section 101.¹⁸³ However, legislative amendments to Section 101 are unlikely to occur anytime soon.¹⁸⁴ Administratively, the USPTO has been fast to react to the Supreme Court's judgement.¹⁸⁵ After the *Mayo* case, the USPTO responded directly to

177. *Id.*

178. *Id.*

179. Susan Moore, *Gartner Says Within 5 Years, Organizations Will be Valued on their Information Portfolios*, GARTNER (Feb. 8, 2017), <https://www.gartner.com/en/newsroom/press-releases/2017-02-08-gartner-says-within-five-years-organizations-will-be-valued-on-their-information-portfolios>.

180. Madigan & Mossoff, *supra* note 171, at 955.

181. Jorge Goldstein et al., *Is It Time to Amend 101?*, IPWATCHDOG (Sept. 25, 2016), <http://ipwatchdog.com/2016/09/25/time-to-amend-101/id=72825>.

182. *AIPLA Legislative Proposal and Report on Patent Eligible Subject Matter*, AM. INTELL. PROP. L. ASS'N 4 (May 12, 2017), <http://aipla.org/resources2/reports/2017AIPLDirect/Documents/AIPLA%20Report%20on%20101%20Reform-5-19-17-Errata.pdf>.

183. Matthew Anderson, *Legislative Changes to 35 U.S.C. § 101*, AM. U. INTELL. PROP. BRIEF (Dec. 7, 2016), <http://www.ipbrief.net/2016/12/07/legislative-changes-to-35-usc-%C2%A7-101/>.

184. Stuart P. Meyer, *Judge Mayer's Concurrence in IV Shows the Problem with Judicially Created Exceptions*, BILSKIBLOG (Oct. 10, 2016), <https://www.bilski.blog.com/2016/10/judge-mayers-concurrence-in-iv-shows-the-problem-with-judicially-created-exceptions-html/>.

185. William C. Rowland, *USPTO Issues New Alice Guidance*, BUCHANNAN INGERSOLL & ROONEY PC (Apr. 26, 2018), <https://www.bipc.com/uspto-issues-new-alice-guidance>.

the ruling with new guidelines.¹⁸⁶ Although originally thought just to cover “natural laws exceptions,” these guidelines have been extended to include an “abstract idea.”¹⁸⁷ If left for the judiciary, this exception must be refined to meet two criteria: First, the standard must uphold the constitutional basis of the patent system; and second, the test must survive the development of all technological areas and prevent the swallowing up any field.¹⁸⁸

2. Abandoning Mayo-Alice Test

Step one of the *Mayo-Alice* test requires determining whether a claim is directed to a judicial exception, such as an abstract idea.¹⁸⁹ This is a rather odd requirement, as “at some level all inventions embody, use, reflect, rest upon, or apply law of nature, natural phenomenon, or abstract idea.”¹⁹⁰ By merely requesting lower courts to look for an abstract idea, absent further guidance, different people will have different perspectives on whether an abstract idea is present.¹⁹¹ In *DDR Holdings v. Hotels.com*, the Federal Circuit completely withdrew from the task of identifying an abstract idea outside the scope of controlling precedent.¹⁹² The inoperability of the *Mayo-Alice* test shows a stark contrast between the United States and Europe: Europe adopts a liberal approach on what is patent eligible and allows the patentability doctrines to further assess whether the invention is patent worthy.¹⁹³ Section 101 now serves not just as the gate keeper for eligibility, but also patentability, covering areas reserved for Sections 102, 103, and 112.¹⁹⁴ Unlike Europe on

186. U.S. PATENT & TRADEMARK OFFICE, 2012 INTERIM PROCEDURE FOR SUBJECT MATTER ELIGIBILITY ANALYSIS OF PROCESS CLAIMS INVOLVING LAWS OF NATURE (July 3, 2012), http://www.uspto.gov/sites/default/files/patents/law/exam/2012_interim_guidance.pdf.

187. *Alice Corp. Pty. v. CLS Bank Int’l*, 134 S. Ct. 2347, 2357 (2014).

188. Busse, *supra* note 104, at 273–74.

189. 2014 Interim Guidance on Patent Subject Matter Eligibility, 79 Fed. Reg. 74618, 74622 (Dec. 16, 2014).

190. *Id.*

191. Gary Montle et al., *Our Patent System and Health Care Information Technology: Valuable Incentive or Impediment to Innovation*, 2 BELMONT L. REV. 93, 112 (2015).

192. *DDR Holdings, LLC v. Hotels.com LP*, 773 F.3d 1245, 1257 (Fed. Cir. 2012) (“identifying the precise nature of the abstract idea is not as straightforward as in *Alice* or some of our other recent abstract idea cases”).

193. James Leach, *Patentability of Software and Business Method Inventions in Europe*, MEWBURN ELLIS, <https://mewburn.com/resource/patentability-of-business-method-and-software-inventions-in-europe-2/> (last visited Aug. 26, 2019).

194. *Remarks by Director Iancu at the 10th Annual Patent Law & Policy*, U.S. PATENT & TRADEMARK OFFICE (Nov. 26, 2018), <https://www.uspto.gov/about-us/news-updates/remarks-director-iancu-10th-annual-patent-law-policy-conference>.

the clarity of the standard, the United States traps itself in the categorical quagmire, and if the issue is unfixable, abandonment might be an option.

3. Section 101—Simply an Inquiry on Man-Made or Not

It does not take a rocket scientist to fix Section 101; one can simply look back into history for guidance. U.S. patent law, unlike the EPC, does not expressly list what inventions are patent ineligible, no matter how meticulous it is.¹⁹⁵ The intention of lawmakers is obvious: patent law is a tool to foster innovation, not to hinder it.¹⁹⁶ The welcoming attitude of the patent system is one of the reasons why the United States surpassed other countries in the race of biotechnology by being the first to recognize man-made bacteria as patent eligible.¹⁹⁷ This liberal attitude only suffers some setback when congress expressly bans patent eligibility on claims directed to, or encompassing, a human organism in Section 33(a) of the America Invents Act.¹⁹⁸ Hence, although not everything under the sun made by man is patentable, absent Congress' express prohibition on other patent ineligible subject matter, shouldn't Section 101 be given a more liberal interpretation rather than looking at whether the claimed invention falls into one of the judicial exception, which almost all inventions certainly will?¹⁹⁹ Anything that is the result of human effort is eligible for patenting. This is the position of Congress, as confirmed by the legislative history of the Patent Act of 1952.²⁰⁰

The requirement of human effort is similar to the EPO's approach in requiring the invention to possess technical means, implicitly indicating that it is not an EPC Article 52(3) patent ineligible subject matter "as such."²⁰¹ The requirement of human effort was made famous during the twilight of the biotech era, where much of the inventions involved might have also been subject matter ineligible because they tended to fall into the excluded subject matter as a "Product of Nature."²⁰² The Product of Nature doctrine was estab-

195. Gene Quinn, *Patentability Overview: When Can an Invention be Patented?*, IP WATCHDOG (June 2, 2018), <http://www.ipwatchdog.com/2017/06/03/patent-ability-invention-patented/id=84071/>.

196. *Id.*

197. *Id.*

198. Leahy-Smith America Invents Act, Pub. L. 112–29, § 33(a) (2011) (“notwithstanding any other provision of law, no patent may issue on a claim directed to or encompassing a human organism”).

199. *Id.*

200. S. REP. NO. 82-1979, at 5 (1952).

201. EPC Article 52(3).

202. *Patentability of Biotech Inventions in USA – Patentable Subject Matter*, BANANAIP (Dec. 27, 2010), <https://www.bananaip.com/ip-news-center/patent-ability-of-biotech-inventions-in-4/>.

lished as a limitation to the broad language of Section 101.²⁰³ In *Funk Brothers Seed Co. v. Kao Inoculant Co.*,²⁰⁴ the Court stated that the non-inhibitive qualities of the bacteria are the work of nature. “The qualities of the bacteria . . . are part of the storehouse of knowledge of all men.”²⁰⁵ “They are manifestation of laws of nature, free to all men are reserved exclusively to none.”²⁰⁶ This statement is strikingly similar to Court’s fear of preemption in *Alice*.²⁰⁷

However, the Supreme Court interpreted the Product of Nature doctrine differently in *Diamond v. Chakrabarty*.²⁰⁸ The Court rejected the PTO’s argument that living organisms are not patentable and held that a living, genetically altered organism may qualify for patent protection as a new “manufacture” or “composition of matter” under Section 101.²⁰⁹ The Court then concluded that Congress intended statutory subject matter to “include anything under the sun that is made by man,”²¹⁰ and patents would not be provided to “hitherto unknown natural phenomenon, but only to “products of human ingenuity.”²¹¹ “Congress thus recognized that the relevant distinction was not between living and inanimate things, but between products of nature, whether living or not, and human-made inventions.”²¹²

4. Summary

In order to foster promising innovation and boost the economy, a clear and operable patent standard is urgently needed. The current *Mayo-Alice* test proves to be inoperable and cumbersome, and creates more issues than it tries to solve. For an era that is built on Big Data and algorithms, the *Mayo-Alice* test has to be abandoned; otherwise, industries might turn toward trade secret instead and further hinder the growth of algorithm economy. Some commentators have argued that the Supreme Court has confused the difference between patent eligibility and patentability,²¹³ while some defended the Supreme Court’s position by focusing on the inventor’s contribution.²¹⁴

203. 2016 PATENT SUBJECT MATTER ELIGIBILITY, MPEP § 2106 (9th ed. Rev. 8, Jan. 2018).

204. 333 U.S. 127, 130 (1948).

205. *Id.*

206. *Id.*

207. *Alice Corp. Pty. v. CLS Bank Int’l*, 134 S. Ct. 2347, 2355 (2014).

208. 447 U.S. 303, 305 (1980).

209. *Id.* at 308–09.

210. *Id.*

211. *Id.* at 309.

212. *Id.* at 313.

213. Taylor, *supra* note 122.

214. Mark A. Lemly et al., *Life after Bilski*, 63 STAN. L. REV. 1315 (2011).

However, focusing on an inventor's contribution at Section 101 basically leaves Section 112 redundant, and the real question is not what the inventor's has contributed in Section 101, but, like EPO, whether it is a man-made invention.²¹⁵ Under this approach, Second Generation Personalized Medicine predictive algorithms will not be denied before the chance to be assessed for patentability.

V. CONCLUSION

In light of the coming age of Second Generation Personalized Medicine, the patent system should be amenable to foster the development of this nascent industry. However, the Supreme Court has been counterproductive by issuing the *Mayo-Alice* test, which, as shown in this article, failed to provide the necessary incentive. The *Mayo-Alice* test is inoperable, expensive, and a doctrinal disaster. The Supreme Court could remedy the mistake simply by looking back to the purpose of Section 101, as Congress originally intended, looking to whether the claimed invention is man-made as the threshold for eligibility requirement before moving to patentability assessment. Following this approach, the Supreme Court would not run into the embarrassment of a doctrinal disaster and would allow inventors the chance to prove the value of their invention without being simply denied at Section 101.

215. This proposal might not be workable when machine learning evolves into "strong AI" or Artificial General Intelligence (AGI), which is when machines achieve consciousness or display intelligence equivalent to that of human. Under this scenario, machines could learn, program, and interact with patients without human intervention. Till this day, artificial intelligence has not reached to this level, but this issue remains a topic for further studies.