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## Essay

# Handling the *Mayo* Powder Keg: Emphasizing Preemption in § 101 Biotechnology Inquiries

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### INTRODUCTION

To incite a jury's emotions, attorneys have stated that the "clear and convincing" evidentiary standard required to invalidate a patent is the same standard of proof required to justify taking a child away from a parent.<sup>1</sup> Although such statements are likely an evidentiary rule violation, the point *is* illustrative of how inventors may feel about their inventions.<sup>2</sup> Some put

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1. *E.g.*, Sealant Sys. Int'l, Inc. v. TEK Global S.R.L., No. 5:11-cv-00774, 2014 WL 1008183, \*7 n.75 (N.D. Cal. Mar. 7, 2014). Whether patentable subject matter is reviewed with the same clear and convincing standard as other invalidity arguments has been debated. Robert Shaffer & Scott Allen, *Section 101 Decisions Clarify 'Clear and Convincing Evidence'*, LAW360 (Mar. 13, 2018), <https://www.law360.com/articles/1021490> [<https://perma.cc/T8BU-5N8C>]. But the Federal Circuit has concluded that "[a]ny fact . . . pertinent to the invalidity conclusion must be proven by clear and convincing evidence" and that "[l]ike indefiniteness, enablement, or obviousness, whether a claim recites patent eligible subject matter is a question of law which may contain underlying facts." *Berkheimer v. HP Inc.*, 881 F.3d 1360, 1368 (Fed. Cir. 2018) (citations omitted).

2. *See* FED. R. EVID. 403; *see also* Defendant Apple Inc.'s Notice of Motion and Motion *In Limine* Nos. 6–10 to Exclude Irrelevant Miscellaneous Evidence at 14–15, *Pinn Inc. v. Apple Inc.*, No. 8:19-cv-01805, 2021 U.S. Dist. LEXIS 200973, (C.D. Cal. Apr. 2, 2021) (seeking to exclude any such comparison to child custody cases); Samsung's Motions *In Limine* and to Exclude at 11–12,

their entire life's work into securing a patent. However, even decades of research and discovery may still not prove adequate to merit the issuance of a patent. The claimed invention must fall within a category of subject matter that is eligible for patenting under 35 U.S.C. § 101. Further, the Supreme Court has staunchly held that even some of the most profound discoveries and exciting scientific advancements may not be eligible for patenting if they are simply an attempt to monopolize a law of nature, natural phenomenon, or abstract idea ("patent-ineligible concepts").<sup>3</sup> Nonetheless, the incredible time and energy put into the scientific research process needs to be respected for a patent system to have any value. There is no better way to respect inventors and their work than to provide them clear and defined rules for what claims describing their inventions will and will not be eligible for patenting.

Unfortunately, it is nearly impossible to find a patent attorney who will agree that the federal courts' current application of § 101 is crystal clear.<sup>4</sup> The modern state of patentable subject matter law derives from the four Supreme Court holdings of *Bilski v. Kappos*,<sup>5</sup> *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*,<sup>6</sup> *Ass'n for Molecular Pathology v. Myriad Genetics Inc.*,<sup>7</sup> and *Alice Corp. v. CLS Bank International* (Mayo and

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Rfeyber Corp. v. Samsung Elecs. Co., No. 2:20-cv-00335, 2021 U.S. Dist. LEXIS 222160 (E.D. Tex. Nov. 17, 2021) (seeking the same); Plaintiff True Chemical Solutions, LLC's Omnibus Motions *In Limine* as to Performance Chemical Company at 10, True Chem. Sols., LLC v. Performance Chem. Co., No. 7-18-cv-00078, 2021 U.S. Dist. LEXIS 42529 (W.D. Tex. Mar. 5, 2021) (seeking the same).

3. *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 577 (2013) ("[B]ut groundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry."). These three listed categories have been determined to be the three that are not patentable. *Id.* at 589.

4. *E.g.*, John M. Golden, *Flook Says One Thing, Diehr Says Another: A Need for Housecleaning in the Law of Patentable Subject Matter*, 82 GEO. WASH. L. REV. 1765, 1765–66 n.2–4 (2014); David O. Taylor, *Confusing Patent Eligibility*, 84 TENN. L. REV. 157, 158–160 (2016); Daniel R. Cahoy, *Patently Uncertain*, 17 NW. J. TECH. & INTELL. PROP. 1, 3 (2019); Jay P. Kesan & Runhua Wang, *Eligible Subject Matter at the Patent Office: An Empirical Study of the Influence of Alice on Patent Examiners and Patent Applicants*, 105 MINN. L. REV. 527, 528–31 (2020).

5. 561 U.S. 593 (2010).

6. 566 U.S. 66 (2012).

7. 569 U.S. 576.

*Alice* being the more prevalent of the four).<sup>8</sup> The test that comes out of these cases has two steps. At step one, a court asks “whether the claims at issue are *directed to* one of those patent-ineligible concepts.”<sup>9</sup> If they are not, the claims are patent eligible.<sup>10</sup> If they are, a court must consider the claims individually and together “to determine whether additional elements ‘transform the nature of the claim’ into a patent-eligible application.”<sup>11</sup> What exactly it means to be “directed to” a patent-ineligible concept and what it means to “transform the nature of the claim” have been left up to the district courts and the Federal Circuit to determine.

After *Alice*, the Court denied petitions having to do with patentable subject matter eligibility.<sup>12</sup> In 2021, there was a new hope that the Court was going to grant a writ of certiorari for what would have likely been another landmark case on the issue.<sup>13</sup> It requested the Solicitor General’s opinion on the case and, after a year of waiting, the opinion recommended the Court take the case.<sup>14</sup> But, in June 2022, the Court ultimately declined to hear the matter.<sup>15</sup> The Court’s rejection inspired Senator

8. 573 U.S. 208 (2014). *Alice* has solidified the *Mayo* test into an articulable two-part analysis.

9. *Vanda Pharms. Inc. v. West-Ward Pharms. Int’l Ltd.*, 887 F.3d 1117, 1134 (Fed. Cir. 2018) (emphasis in original) (citing *Alice*, 573 U.S. at 217).

10. *Id.*

11. *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1375 (2015) (citing *Mayo*, 566 U.S. at 78).

12. *E.g.*, *Sequenom, Inc. v. Ariosa Diagnostics, Inc.*, 579 U.S. 928 (2016); *Hikma Pharms. USA Inc. v. Vanda Pharms. Inc.*, 140 S. Ct. 911 (2020).

13. Blake Brittain, *U.S. Supreme Court Asks for Solicitor General’s Take on Patent-Eligibility Case*, REUTERS (May 3, 2021) (citing *Am. Axle & Mfg. v. Neapco Holdings LLC*, 977 F.3d 1379 (Fed. Cir. 2020)), <https://www.reuters.com/legal/government/us-supreme-court-asks-solicitor-generals-take-patent-eligibility-case-2021-05-28> [<https://perma.cc/3FTY-STUE>].

14. Eileen McDermott, *Solicitor General Tells SCOTUS CAFC Got it Wrong in American Axle, Recommends Granting*, IP WATCHDOG (May 24, 2022), <https://www.ipwatchdog.com/2022/05/24/solicitor-general-tells-scotus-cafc-got-wrong-american-axle-recommends-granting/id=149248> [<https://perma.cc/MTK7-CTLW>].

15. Brad M. Scheller, Andrew H. DeVoogd & Matthew A. Karambelas, *SCOTUS Declines to Answer Calls for Clarification in American Axle v. Neapco*, NAT’L L. REV. (July 13, 2022), <https://www.natlawreview.com/article/scotus-declines-to-answer-calls-clarification-american-axle-v-neapco> [<https://perma.cc/M46U-HRPJ>].

Thom Tillis to introduce a significant amendment to § 101 in August 2022.<sup>16</sup> Senator Tillis's proposed bill included specific categories of discovery that cannot be patented and provided criteria for the courts to weigh when considering patent eligibility.<sup>17</sup> The bill was applauded by intellectual property attorneys and judges as a much needed solution to the uncertainty in patent eligibility.<sup>18</sup> At present, however, the future of the bill is unclear.<sup>19</sup>

One of the greatest difficulties in creating a uniform system on patent eligibility is that each field of innovation flirts with ineligibility in its own way.<sup>20</sup> This means that drafting one-size fits all legislation can be hard to do. It is thus important for legislators to consider each field separately and how the proposed legislation will affect that field. The purpose of this Essay is to analyze how the *Mayo/Alice* framework is being applied in the field of biotechnology at the Federal Circuit level and to highlight the Federal Circuit's inconsistencies when applying the framework within that discipline. Through this analysis the goals of the Essay are twofold: first, to show why a bill like Senator Tillis's is needed and second, to provide a recommendation for how a proposed bill could best serve the biotechnology field.

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16. *Tillis Introduces Landmark Legislation to Restore American Innovation*, THOM TILLIS (Aug. 3, 2022), <https://www.tillis.senate.gov/2022/8/tillis-introduces-landmark-legislation-to-restore-american-innovation> [https://perma.cc/A2EZ-E9ED].

17. Patent Eligibility Restoration Act, S. 4734, 117th Cong. (2022).

18. *E.g.*, Gene Quinn, *Tillis' Promised Patent Eligibility Bill Would Overrule Myriad*, Mayo, IP WATCHDOG (Aug. 3, 2022) (quoting retired Federal Circuit judge Kathleen O'Malley), <https://www.ipwatchdog.com/2022/08/03/tillis-patent-eligibility-bill-overrule-myriad-mayo/id=150586> [https://perma.cc/5QEQ-URDU]; Angela Morris, *Tillis' 101 Reform Bill Wins Plaudits Despite Flaws*, IAM (Aug. 3, 2022), <https://www.iam-media.com/article/tilliss-101-reform-bill-wins-plaudits-despite-flaws> [https://perma.cc/3N7F-4C4C].

19. In an interview with IP Watchdog, Senator Tillis addressed criticism of his bill in part by stating the bill was just "a starting point" and that "all ideas can and should be on the table." Gene Quinn & Eileen McDermott, *Tillis Addresses Criticism of His Eligibility Reform Bill, Warns WD of TX Not to Backtrack on Standing Order*, IP WATCHDOG (Aug. 31, 2022), <https://www.ipwatchdog.com/2022/08/31/tillis-addresses-criticism-eligibility-reform-bill-warns-wd-tx-not-backtrack-standing-order/id=151211> [https://perma.cc/Y43H-DDT5]. This indicates that even Senator Tillis expects the bill to change before it gets through the legislative process.

20. For example, biotechnology cases often inquire into whether the patent is seeking to patent a natural phenomenon; whereas software related patents often inquire into whether the patent is seeking to patent an abstract idea.

This Essay ultimately asserts that the Federal Circuit’s incorporation of the *Mayo/Alice* “two-step” test proves it to be a confusing test for inventors to follow and blurs the line of becoming a §§ 102 and 103 inquiry into novelty and obviousness.<sup>21</sup> At step one, the Federal Circuit has created a confusing standard for what it means for a claim to be “directed to” patent eligible subject matter. At step two, the consideration of “what the claims add” has created a near impossible bar for biotechnology patents to overcome. The Essay further endorses Senator Tillis’s proposed amendment as it pertains to doing away with this quasi-§§ 102, 103 standard. Although this Essay agrees the *Mayo/Alice* framework has caused disarray, the *Mayo* Court was correct in its recognition of the importance of “preemption” in the § 101 inquiry.<sup>22</sup> Unfortunately, it was not emphasized enough for the Federal Circuit to give the concept the proper weight in its analyses. Therefore, this Essay further recommends that—to create more clarity—the proposed legislation should incorporate an emphasis on the importance of preemption in the § 101 inquiry.

Part I provides a more detailed background of how the *Mayo/Alice* framework developed. Part II evaluates the “biotechnology-patentable subject matter” cases heard by the Federal Circuit since *Alice*. It explains how—in practice—the *Mayo/Alice* framework has created both unwanted confusion at step one and unwanted consistency of result at step two. Part III explains how preemption emphasis reconciles the Federal Circuit cases, points out which cases were flawed, and creates a more consistent standard going forward. Such emphasis could help better amend Senator Tillis’s proposed bill should it move forward in the legislative process.

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21. 35 U.S.C. §§ 102 (novelty), 103 (obviousness); *see also* 2 CHISUM ON PATENTS § 3.01 (“An invention must be new at the time of discovery by an original inventor to be patentable. Simply put, an invention is not new, that is, it is ‘anticipated,’ if the invention is disclosed in the prior art.”); 2 CHISUM ON PATENTS § 5.01 (“Nonobviousness . . . means that an invention must not have been obvious . . . at the time of invention . . . in light of the prior art. Nonobviousness is distinct from novelty in the sense that an invention may be obvious even though it is not identically disclosed anywhere in the prior art.”).

22. *See infra* Part I.B.2 for an explanation on the premise of preemption.

I. A BRIEF HISTORY OF *BILSKI*, *MAYO*, *MYRIAD*, AND *ALICE*A. THE FUSE: *BILSKI*

*Bilski* was the fuse that started the revamp of subject matter eligibility jurisprudence.<sup>23</sup> There, the Supreme Court analyzed a patent for an invention that “explain[ed] how buyers and sellers of commodities in the energy market [could] protect, or hedge, against the risk of price changes.”<sup>24</sup> The majority opinion spent little time talking about the invention itself.<sup>25</sup> Instead, the Court spent several pages writing about the use of the “machine-or-transformation” test that had been declared by the Federal Circuit as the exclusive test to be used when examining subject-matter eligibility.<sup>26</sup>

The “machine-or-transformation” test held that a claimed process was patent eligible “if: ‘(1) it [was] tied to a particular machine or apparatus, or (2) it transform[ed] a particular article into a different state or thing.’”<sup>27</sup> Although the Supreme Court agreed that this was a useful test when evaluating the eligibility of a patent, it noted that the Federal Circuit was wrong in declaring that it was the *sole* test to apply in a patentable subject matter inquiry.<sup>28</sup> The Supreme Court refused to say anything more, other than that the “machine-or-transformation” test was a useful *clue* in the determination of a patent’s eligibility.<sup>29</sup> Ultimately though, the Supreme Court agreed with the Federal Circuit that the method at hand was too abstract in light of case precedent to be considered patent eligible.<sup>30</sup>

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23. *Bilski v. Kappos*, 561 U.S. 593 (2010).

24. *Id.* at 599.

25. *Id.* at 609–13.

26. *Id.* at 599–609.

27. *Id.* at 600 (citing *In re Bilski*, 545 F.3d 943, 959–60 (Fed. Cir. 2008)).

28. *Id.* at 603 (“Adopting the machine-or-transformation test as the sole test for what constitutes a ‘process’ (as opposed to just an important and useful clue) violates these statutory interpretation principles.”).

29. *Id.* at 604 (citing *Gottschalk v. Benson*, 409 U.S. 63, 71 (1972)) (“At the same time, [the Court] explicitly declined to ‘hold that no process patent could ever qualify if it did not meet machine or transformation requirements.’”).

30. *Id.* at 609.

B. THE POWDER KEG: *MAYO*

## 1. Setting Aside the Machine-or-Transformation Test and Creating a “Two-Step” Test

If *Bilski* was the fuse, *Mayo* was the powder keg that re-wrote patentable subject-matter law. The patent there involved the use of thiopurine drugs in the treatment of autoimmune diseases.<sup>31</sup> The claim had only three steps: (1) administering a drug; (2) determining the level of metabolite the subject’s body produced; and (3) declaring what pre-specified levels indicated a need to increase or decrease the dose of drug used.<sup>32</sup> This was the second time the Supreme Court had seen the case.<sup>33</sup> In its first bout, the Court remanded the case back to the Federal Circuit and reiterated its rejection of the “machine-or-transformation” test as the sole test to be used to decide patent eligibility.<sup>34</sup> On remand, the Federal Circuit still found that the plaintiff’s claimed method was patent eligible even when applying the “machine-or-transformation” test as a clue as opposed to a determining test.<sup>35</sup>

Upon review of the Federal Circuit’s second decision, the Supreme Court no longer seemed interested in even considering the “machine-or-transformation” test.<sup>36</sup> The Court asked: “[D]o the patent claims add *enough* to their statements . . . to allow the processes they describe to qualify as patent-eligible processes that *apply* natural laws?”<sup>37</sup> The Court said that the claims needed to do more than describe a natural law and then “apply

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31. *Mayo Collaborative Servs. v. Prometheus Lab’ys, Inc.*, 566 U.S. 66, 73 (2012).

32. An observed metabolite level below 230 pmol per  $8 \times 10^8$  red blood cells indicated a need for an increase in the dose and a level above 400 pmol per  $8 \times 10^8$  red blood cells indicated a need for a decrease in the dose. *Id.* at 74–75.

33. *Prometheus Lab’ys, Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336 (Fed. Cir. 2009); *Mayo Collaborative Servs. v. Prometheus Lab’ys, Inc.*, 561 U.S. 1040 (2010).

34. *Mayo*, 561 U.S. at 1040.

35. *Prometheus Lab’ys, Inc. v. Mayo Collaborative Servs.*, 628 F.3d 1347, 1355 (Fed. Cir. 2010).

36. In fact, the Supreme Court all but overruled the “machine-or-transformation” test. *Mayo*, 566 U.S. at 88 (“Regardless, in stating that the ‘machine-or-transformation’ test is an ‘important and useful clue’ to patentability, we have neither said nor implied that the test trumps the ‘[a] of nature’ exclusion.”) (emphasis in original) (citing *Bilski v. Kappos*, 531 U.S. 593, 603 (2010)).

37. *Id.* at 77 (emphasis in original).

it.”<sup>38</sup> The claims needed to “transform an unpatentable law of nature into a patent eligible application of such a law.”<sup>39</sup> As part of the analysis, the Court looked at each of the claimed steps individually and then at the claim in its entirety.<sup>40</sup> It then rationalized its decision to create a new test to examine patentable subject matter by relying on the case precedent of *Parker v. Flook* and *Diamond v. Diehr*.<sup>41</sup>

## 2. Emphasizing the Premise of “Preemption”

The test that came out of *Mayo* was significant because lower courts were instructed to focus on whether the claim was pointed at a law of nature, natural phenomenon, or abstract idea, and then determine if there was something more added to the claim that went beyond saying “apply this law.” The underlying concern of this assertion is that of preemption. This premise can be traced back to *O’Reilly v. Morse* when the famous inventor Samuel Morse’s patent was at issue.<sup>42</sup> Although not a subject matter eligibility case, the patent was held invalid because it attempted to cover all future inventions relating to its claimed telegraph technology and preempt others from working in the field.<sup>43</sup> The Court carried the principles of *Morse* into the

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38. *Id.* at 72.

39. *Id.* at 79 (citing *Parker v. Flook*, 437 U.S. 584, 590 (1978)).

40. *Id.* at 78–80.

41. *Id.* at 80–82; *see also* *Diamond v. Diehr*, 450 U.S. 175 (1981); *Flook*, 437 U.S. 584. *Diehr* examined a claimed invention that integrated the Arrhenius equation with a process to cure rubber in a mold. *Diehr*, 450 U.S. at 177–78. *Flook* involved a claimed invention that adjusted alarm limits in the catalytic conversion of hydrocarbons by (1) measuring the level of a variable; (2) inputting that variable into an equation to test the alarm limit; and (3) adjusting the system to reflect the new alarm-limit value. *Flook*, 437 U.S. at 585–87. The Court found the former patentable but the latter not. *Mayo*, 566 U.S. at 80–81. In distinguishing the cases, the *Mayo* Court held that the claimed invention in *Flook* did not “explain how the variables used in the formula were to be selected, nor did the [claim] contain any disclosure relating to the chemical processes at work or the means of setting off an alarm or adjusting the alarm limit.” *Id.* at 81 (citing *Diehr*, 450 U.S. at 192). It should be noted that the *Mayo* Court did have to craft a difference between these two cases as Justice Rehnquist wrote the majority opinion in *Diehr* but was one of the dissenters in *Flook*. *See* Golden, *supra* note 4, at 1781–82.

42. 56 U.S. (15 How.) 62 (1854).

43. *Id.* at 120.



§ 101 inquiry in *Flook* and *Diehr*.<sup>44</sup> It recognized that every invention incorporates unpatentable principles into it.<sup>45</sup> But the central goal under the premise of preemption is to ensure that an inventor does not find a way to patent those underlying unpatentable principles and laws under the guise of a greater invention in order to keep other inventors from using them in future innovation.<sup>46</sup>

### C. INSIGHT INTO TRANSFORMATION: *MYRIAD*

In *Myriad*, the Supreme Court examined two different patents.<sup>47</sup> The first was directed at an isolated DNA sequence of a specific gene.<sup>48</sup> The second was directed at a manufactured form of DNA that lacked the introns normally observed in nature (cDNA).<sup>49</sup> The Court held that the former was patent ineligible but that the latter was eligible.<sup>50</sup> The Court's reasoning was that the DNA sequence, although isolated from the rest of the genome, was something that occurred in nature.<sup>51</sup> The isolation itself was not enough to transform the natural product into something that could be patented; the patent was claiming the natural product itself.<sup>52</sup> The Court also pointed out that—if the patent was considered patent eligible for simply isolating the desired DNA segment—a “would-be-infringer” could simply isolate

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44. *Flook*, 437 U.S. at 590–92, 595; *Diehr*, 450 U.S. at 188. The *Mayo* court also recognized *Morse* in its analysis. *Mayo*, 566 U.S. at 72 (“[Precedent] warn[s] us against upholding patents that claim processes that too broadly pre-empt the use of a natural law.”) (citing *Morse*, 56 U.S. (15 How.) at 112–20).

45. *Mayo*, 566 U.S. at 71 (“For all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas.”).

46. *Id.* at 72, 81 (“And so the patentees did not ‘seek to pre-empt the use of [the] equation,’ but sought ‘only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process.’”) (citing *Diehr*, 450 U.S. at 187).

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

48. *Id.* at 580.

49. *Id.* Introns are the noncoding sections found in DNA and RNA that are naturally spliced out as RNA is translated into a protein. *Definition: Intron/Introns*, SCITABLE BY NATURE EDUC., <https://www.nature.com/scitable/definition/intron-67> [<https://perma.cc/XHN8-5Z4Z>]. Conversely, exons contain the coding region and therefore are the portion most often sought-after by scientists. *Id.*

50. *Myriad*, 569 U.S. at 580.

51. *Id.* at 593.

52. *Id.*

the same part of the genome with a few added nucleotides, making a similar yet “unique” molecule that effectively copied Myriad’s patented DNA sequence.<sup>53</sup> If Myriad were to sue such “would-be-infringer” for infringement it would have to argue that what was actually claimed in its patent was not a unique molecule but the underlying DNA segment desired (i.e., the natural phenomenon which itself is ineligible for patenting).<sup>54</sup> This would have been an absurd result.

The Court then moved on to the patentability of cDNA and found that its creation was patent eligible.<sup>55</sup> In coming to this conclusion, the Court focused on the fact that, unlike the isolated DNA analyzed first, cDNA is never produced naturally and therefore the patent was not directed at an ineligible concept.<sup>56</sup> The opinion did little to add to the test that was articulated in *Mayo* but it provided some insight into how it should be applied and gave examples of a valid claim under § 101.

#### D. CLEANING UP AND ARTICULATING THE POWDER KEG: ALICE

*Alice* involved a patent for “a computer-implemented scheme for mitigating ‘settlement risk’ (i.e., the risk that only one party to a financial transaction will pay what it owes) by using a third-party intermediary.”<sup>57</sup> The Court began its analysis by emphasizing the importance of preventing the preemption of the use of the “basic tools of scientific and technological work” and the “building blocks of human ingenuity.”<sup>58</sup> It further stated

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53. *Id.*

54. *Id.*

55. *Id.* at 594–95.

56. *Id.* at 595. (“[A] lab technician unquestionably creat[ed] something new when [the] cDNA [was] made.”). This seemed to be a regression back to the “machine-or-transformation” test. It is arguable that the Court was implicitly applying that test as a *clue* to determining patentability. However, as will be discussed further, the Federal Circuit’s application of the *Mayo/Alice* framework likely would not allow a claim over cDNA to stand if *Myriad* had not been decided. *See infra* Part III.B.1. Simply put, if *Myriad* was never analyzed by the Supreme Court and instead was put before the Federal Circuit in 2020, the Federal Circuit may have agreed that the cDNA claim passes the “machine-or-transformation” test but it likely would have found it failed the *Mayo/Alice* test. And from the Supreme Court precedent of *Mayo*, it would have determined that the latter test trumps the former. Nonetheless, this is purely speculative.

57. *Alice Corp. v. CLS Bank Int’l*, 573 U.S. 208, 212–13 (2014).

58. *Id.* at 216.

that the goal of the § 101 analysis is to “distinguish between patents that claim the ‘building blocks’ of human ingenuity and those that integrate the building blocks into something more.”<sup>59</sup>

To make this distinction, the Court attempted to articulate its test from *Mayo* by breaking it into a set, two-step procedure. At step one, a court “determine[s] whether the claims at issue are directed to [a] patent-ineligible concept.”<sup>60</sup> If the claim is not directed at such a concept, then the analysis ends, and the claims are patentable under § 101.<sup>61</sup> If the claim is directed at such a concept, the court asks, “what else is there in the claims before [the court].”<sup>62</sup> Walking through the analysis of the patent at issue, the Court determined that the claims were directed at the abstract idea of settlement negotiations and that the only “inventive concept” to transform the claims was the addition of a computer.<sup>63</sup> The Court felt that the addition of a computer to the abstract idea was not enough to transform a claim into a patent eligible thing.<sup>64</sup> It further found that rejecting the addition of a computer to patent eligibility was in accord with the preemption concern.<sup>65</sup> In sum, the Court solidified its *Mayo* precedent into a two-step test that all but explicitly overruled the “machine-or-transformation” test.

## II: HOW THE FEDERAL CIRCUIT HAS APPLIED THE MAYO/ALICE PRECEDENT TO BIOTECHNOLOGY CASES

Since the *Alice* decision, the Federal Circuit has heard roughly fifteen cases that pertained to § 101 analyses directed at an invention in the biotechnology field.<sup>66</sup> For the most part the

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59. *Id.*

60. *Id.* at 217. This would include natural laws, natural phenomena, and abstract ideas.

61. *Id.*

62. *Id.*

63. *Id.* at 221–22.

64. *Id.* at 222.

65. *Id.* at 223–24 (“This conclusion accords with the pre-emption concern that undergirds our § 101 jurisprudence. Given the ubiquity of computers, wholly generic computer implementation is not generally the sort of ‘additional featur[e]’ that provides any ‘practical assurance that the process is more than a drafting effort designed to monopolize the [abstract idea] itself.’”).

66. *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015); *Genetic Techs. Ltd. v. Merial LLC*, 818 F.3d 1369 (Fed. Cir. 2016); *Rapid Litig. Mgmt. Ltd. v. CellzDirect, Inc.*, 827 F.3d 1042 (Fed. Cir. 2016); *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352 (Fed. Cir. 2017); *Roche Molecular Sys., Inc. v. Cepheid*, 905 F.3d 1363 (Fed. Cir. 2018); *Vanda*

Federal Circuit has followed the two-part analysis of *Mayo* and *Alice*. Consequentially, the Federal Circuit's attempt to strictly adhere to the *Mayo/Alice* framework has shown that its application has created confusing outcomes. For all fifteen cases, the court started at step one and determined the "direction" of the claims (though the court has created a puzzling standard at this step and it is unclear if the analysis of "direction" is pointed at the concept itself or how that concept is being used). At step two, the court has started to do a quasi-§§ 102, 103 analysis that has created an impassable barrier rather than a distinctive hurdle to overcome.

These assertions are supported by an analysis of which step (of the two) the court has found patent eligibility in the cases. In all of the biotechnology cases discussed in this Essay, the Federal Circuit has either found that the patent was valid under § 101 because it passed step one of the test—and was not directed at ineligible subject matter—or it found the invention invalid after performing a step one and step two analysis. Indeed, of the cases analyzed, no patent was determined to be directed at unpatentable subject matter at step one, yet did enough to "transform" the claim and pass step two.<sup>67</sup> This trend is significant. Statistically, a biotechnology patent that is before the Federal Circuit and found to be directed to "ineligible subject matter" is almost certainly dead-on-arrival at step two.

Therefore, inventors want to ensure that the patent claims describing their inventions are not directed to ineligible subject matter so their invention can pass step one and not risk facing

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Pharms. Inc. v. West-Ward Pharms. Int'l Ltd., 887 F.3d 1117 (Fed. Cir. 2018); Athena Diagnostics, Inc. v. Mayo Collaborative Servs., 915 F.3d 743 (Fed. Cir. 2019); Endo Pharms. Inc. v. Teva Pharms. USA, Inc., 919 F.3d 1347 (Fed. Cir. 2019); Genetic Veterinary Scis., Inc. v. Laboklin GmbH & Co. KG, 933 F.3d 1302 (Fed. Cir. 2019); INO Therapeutics LLC v. Praxair Distrib. Inc., 782 F. App'x 1001 (Fed. Cir. 2019); Nat. Alts. Int'l, Inc. v. Creative Compounds, LLC, 918 F.3d 1338 (Fed. Cir. 2019); Boehringer Ingelheim Pharms. Inc. v. Mylan Pharms. Inc., 803 F. App'x 397 (Fed. Cir. 2020); Illumina, Inc. v. Ariosa Diagnostics, Inc., 967 F.3d 1319 (Fed. Cir. 2020); XY, LLC v. Trans Ova Genetics, LC, 968 F.3d 1323 (Fed. Cir. 2020); CareDx, Inc. v. Natera, Inc., 40 F.4th 1371 (Fed. Cir. 2022). There were also three cases in between *Mayo* and *Alice*. *PerkinElmer, Inc. v. Intema Ltd.*, 496 F. App'x 65 (Fed. Cir. 2012); *In re Roslin Inst. (Edinburgh)*, 750 F.3d 1333 (Fed. Cir. 2014); *In re BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litig.*, 774 F.3d 755 (Fed. Cir. 2014); see also *Biotechnology*, BLACK'S LAW DICTIONARY (11th ed. 2019) ("A branch of molecular biology dealing with the use of biological processes to produce useful medical and industrial materials.").

67. For a list of cases analyzed see *supra* note 66 and accompanying text.

the deadly step two. Unfortunately, the lack of clarity on what it means to be “directed to” patent ineligible subject matter does little to help inventors. Not only does this create confusion for inventors, it creates a confusing standard for lower courts to know when they are supposed to perform the second step of the analysis or disregard it.

#### A. THE FEDERAL CIRCUIT’S APPLICATION OF THE *MAYO/ALICE* FRAMEWORK

##### 1. Step One: Looking for Direction? Or Just Creating Categories of Invention?

Step one of the *Mayo/Alice* framework calls for determining if the claims are “directed to” patent ineligible subject matter (i.e., natural laws, phenomena, or abstract ideas).<sup>68</sup> Unfortunately, the Supreme Court never explained what it means for something to be “directed to” patent ineligible subject matter. For the most part, the Federal Circuit has not definitively expanded on any such analysis either. Rather, the Federal Circuit has seemingly created a pattern of distinguishing claims directed to treatment and claims directed to diagnosis (and a lesser category of claims directed to a method of preparation). This is highlighted by Judge Lourie’s opinion in *Illumina, Inc. v. Ariosa Diagnostic, Inc.*, where he attempted to articulate the pattern.<sup>69</sup>

The categories Lourie mentioned included “diagnostic claims,” “treatment claims,” and the new “preparation claims.”<sup>70</sup> Lourie’s first category included cases involving patents for (1) a method that observed muscle-specific tyrosine kinase (MuSK) antibodies<sup>71</sup> and (2) a method that analyzed the correlation between the naturally occurring enzyme myeloperoxidase (MPO)

68. *Alice*, 573 U.S. at 218.

69. *Illumina*, 967 F.3d at 1325.

70. *Id.*

71. *Athena*, 915 F.3d 743. MuSK is found in all human beings and is “crucial to the development and maintenance of the neuromuscular junction” thus making it essential for human movement. Lucia S. Borges & David P. Richman, *Muscle-Specific Kinase Myasthenia Gravis*, 11 FRONTIERS IN IMMUNOLOGY 1, 1 (2020). When the body produces these “MuSK antibodies,” they attack the MuSK causing motor deficiencies (this is a basic definition of an autoimmune disorder). Werner Hoch, John McConville, Sigrun Helms, John Newsom-Davis, Arthur Melms & Angela Vincent, *Auto-Antibodies to the Receptor Tyrosine Kinase MuSK in Patients with Myasthenia Gravis Without Acetylcholine Receptor Antibodies*, 7 NATURE MED. 365, 365 (2001) (disclosing the discovery that was the foundation of the patent in the case).

and the risk for heart disease.<sup>72</sup> In the second category—methods of treatment—Lourie included patents for: (1) a method that determined a patient’s oxymorphone metabolism and prescribed an increase or decrease in dose,<sup>73</sup> (2) a method that delivered an amount of supplement that contained beta-alanine,<sup>74</sup> and (3) a method that delivered a specified amount of iloperidone to schizophrenia patients based on their genotype.<sup>75</sup>

When examining the patent at hand in *Illumina* (involving a method for the separation of maternal and fetal DNA), Lourie declared that its claims fell into the new third category: methods of preparation.<sup>76</sup> The court then found the claims to be valid at step one.<sup>77</sup> The claims that Lourie labeled as “treatment” or “preparation” have been found to be valid at step one for not being “directed to” patent ineligible subject matter. In contrast, all claims labeled “diagnostic” have had to withstand a step two analysis. And thus far none have passed, though Lourie failed to take note of this significant fact.<sup>78</sup> Lourie’s categories indicate that “directed to” does not necessarily mean what the invention claims incorporate, or what the key underlying components

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72. *Cleveland Clinic Found. v. True Health Diagnostics LLC*, 859 F.3d 1352 (Fed. Cir. 2017). Judge Moore also included several others in her analysis in *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 927 F.3d 1333, 1352–53 (Fed. Cir. 2019) (citing *Roche Molecular Sys., Inc. v. Cepheid*, 905 F.3d 1363 (Fed. Cir. 2018) (claiming a method for identifying 11 “fingerprint” markers in MTB); *Genetic Techs. Ltd. v. Merial LLC.*, 818 F.3d 1369 (Fed. Cir. 2016) (claiming a method for amplifying and analyzing introns to determine where an allele was); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015) (claiming a method to amplify cell-free fetal DNA (cffDNA) in a sample); *In re BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litig.*, 774 F.3d 755 (Fed. Cir. 2014) (claiming a method for comparing mutations in DNA strands)).

73. *Endo Pharms. Inc. v. Teva Pharms. USA, Inc.*, 919 F.3d 1347 (Fed. Cir. 2019).

74. *Nat. Alts. Int’l, Inc. v. Creative Compounds, LLC*, 918 F.3d 1338 (Fed. Cir. 2019).

75. *Vanda Pharms. Inc. v. West-Ward Pharms. Int’l Ltd.*, 887 F.3d 1117 (Fed. Cir. 2018).

76. *Illumina, Inc. v. Ariosa Diagnostics, Inc.*, 967 F.3d 1319, 1325 (Fed. Cir. 2020) (“The claims in this case do not fall into either category, and we consider the claims under the *Alice/Mayo* test.”).

77. *Id.* at 1330.

78. Lourie’s findings were consistent with this Essay’s analysis, though the opinion mentioned far fewer cases.

are.<sup>79</sup> Rather, by Lourie’s account, “directed to” means what the claims are attempting to achieve.

## 2. Step Two: Seeking “Something More”

The Supreme Court stated that even if something is directed to patent ineligible subject matter, it can still be patentable if it “transform[s] the nature of the claim” into patent eligible subject matter.<sup>80</sup> The Court then held that the claims should be looked at individually and in their entirety to find an inventive concept.<sup>81</sup>

For the most part, the Federal Circuit has followed this instruction strictly and really homed in on the inventive concept portion of the *Alice* analysis, even to the point of recognizing a blur in the line of analyses between § 101 and §§ 102 (novelty) and 103 (obviousness).<sup>82</sup> Indeed, the Federal Circuit has consistently looked to past, well-known techniques and attempted to determine if those techniques were simply being applied to the natural phenomenon or law.<sup>83</sup>

### B. THE CONFUSING STANDARD CREATED BY THE TEST’S APPLICATION

The Federal Circuit has seemingly applied the *Mayo/Alice* framework properly, but its application has highlighted the framework’s flaws. This “two-step” test has almost been merged into a single step of inquiring as to whether the claims do enough

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79. Surely, MuSK antibodies and beta-alanine are both naturally occurring products. See *supra* note 71 and accompanying text; Eric T. Trexler et al., *International Society of Sports Nutrition Position Stand: Beta Alanine*, 12 J. INT’L SOC’Y SPORTS NUTRITION 1, 1 (2015) (“Beta-alanine is a non-proteogenic amino acid that is produced endogenously in the liver.”).

80. *Alice Corp. v. CLS Bank Int’l*, 573 U.S. 208, 217 (2014).

81. *Id.* The *Alice* Court highlighted that simply adding a computer to help use an equation was not enough of an inventive concept. *Id.* at 223–24.

82. See *Exergen Corp. v. Kaz USA, Inc.*, 725 F. App’x 959, 976 (Fed. Cir. 2018) (Hughes, J., dissenting) (citing *Mayo Collaborative Servs. v. Prometheus Lab’ys, Inc.*, 566 U.S. 66, 90 (2012)) (“To overcome the claimed invention’s lack of an inventive concept, the majority opinion erroneously conflates step two with a novelty inquiry.”).

83. *E.g.*, *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1377 (Fed. Cir. 2015) (finding metabolite determination and the use of PCR “well known” in science); *Genetic Techs. Ltd. v. Merial LLC*, 818 F.3d 1369, 1377 (Fed. Cir. 2016) (finding amplification of genomic DNA with a primer pair indisputably “well known” in the field of molecular biology); *Athena Diagnostics, Inc. v. Mayo Collaborative Servs.*, 915 F.3d 743, 755 (Fed. Cir. 2019) (“[T]he specification describes 125I labeling as a standard practice in a well-known assay.”).

to transform the patent ineligible concept into something patent eligible. Additionally, when doing its analysis of this “single step” test, the Federal Circuit has gone too far and pushed the boundary into the realm of doing a novelty and obviousness analysis under the guise of § 101, which has created confusion. Finally, the Federal Circuit has ignored the concerns of the Supreme Court that the ultimate inquiry for § 101 is whether the patent preempts use of such a natural law or phenomenon in other inventions.

#### 1. Issues with “Direction”

As Lourie noted in the *Illumina* opinion, no diagnostic claim has been held to be patent eligible, but all treatment claims have been held to be patent eligible.<sup>84</sup> But it was not emphasized that among the patents exemplified by the *Illumina* court that were found eligible, *all* were found eligible at step one of the *Mayo/Alice* test. All those that were found ineligible (obviously) failed both steps. No patent was found to fail step one and pass step two. This fact suggests that there should be a clear reason for finding that diagnostic test claims are directed at ineligible subject matter and treatment claims are directed at eligible matter. However, no such clarity is anywhere to be found.

This confusing standard can be exemplified through comparison of the *Illumina*<sup>85</sup> case and *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*<sup>86</sup> Both *Ariosa* and *Illumina* involved cell-free fetal DNA (cffDNA).<sup>87</sup> In *Ariosa*, the patent claimed a method of amplification of cffDNA that was discovered to be present in pregnant mothers’ blood.<sup>88</sup> The court found that the claims were certainly directed at cffDNA (i.e., a natural phenomenon).<sup>89</sup> It then eventually found that the amplification techniques (including standard PCR) were too generally well known to qualify as a

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84. *Illumina, Inc. v. Ariosa Diagnostic, Inc.* 967 F.3d 1319, 1325 (Fed. Cir. 2020).

85. *Id.*

86. 788 F.3d at 1376.

87. *Id.* at 1373; *Illumina*, 967 F.3d at 1322. During pregnancy, some of the unborn child’s DNA (the cffDNA) floats in circulation within the mother’s blood stream and it is commonly extracted for screening tests to see if the child has a genetic disorder like Down syndrome or other trisomy. *Prenatal Cell-Free DNA Screening*, MEDLINEPLUS, <https://medlineplus.gov/lab-tests/prenatal-cell-free-dna-screening> [<https://perma.cc/22K3-ZUPF>].

88. *Ariosa*, 788 F.3d at 1373–74.

89. *Id.* at 1376.



transformation of the claims.<sup>90</sup> In contrast, the *Illumina* court analyzed a claim that addressed a problem found in regard to cffDNA amplification; the cffDNA was hard to distinguish from the mothers' DNA.<sup>91</sup> Upon further examination, the inventors discovered that the cffDNA was of relatively small size (500 base pairs or less) in comparison to the mothers' DNA (greater than 500 base pairs) in the plasma sample.<sup>92</sup> The claims thus described a method of sorting the maternal DNA from the cffDNA.<sup>93</sup> The court here reasoned that the claims were not directed at this natural phenomenon of cffDNA, rather the claims were directed at a *method* of sorting the cffDNA from the mothers' DNA which itself was not ineligible subject matter.<sup>94</sup> In making this determination, the *Illumina* court focused on a finding that the size separation employed "human-engineered parameters that optimize[d] the amount of maternal DNA . . . removed from the mixture and the amount of fetal DNA that remain[ed] in the mixture in order to create an improved end product that [was] more useful for genetic testing than the original natural extracted blood sample."<sup>95</sup>

This Essay does not assert that the overall outcomes of these cases cannot be reconciled. Rather, it more simply asserts that the findings at step one cannot be. The Federal Circuit declared the *Ariosa* claims to be "directed to" the natural phenomenon of cffDNA but declared the *Illumina* claims "directed to" a method of sorting. But, to take the words of the *Ariosa* opinion, a "method [that] begins and ends with a natural phenomenon" is directed at the natural phenomenon.<sup>96</sup> In both cases, the end product was a more accessible sample of the cffDNA taken from the maternal plasma. Thus, the distinction for why the claims should not have *both* been said to be directed to cffDNA lies with Lourie's "direction" at how the natural phenomenon was used as opposed to the

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90. *Id.* at 1377. "PCR" stands for "polymerase chain reaction" an essential and widely used "laboratory technique for rapidly producing (amplifying) millions to billions of copies of a specific segment of DNA, which can then be studied in greater detail." *Polymerase Chain Reaction (PCR)*, NAT'L HUMAN GENOME RSCH. INST., <https://www.genome.gov/genetics-glossary/Polymerase-Chain-Reaction> [<https://perma.cc/88AB-3FP2>].

91. *Illumina*, 967 F.3d at 1322.

92. *Id.*

93. *Id.* at 1323.

94. *Id.* at 1326.

95. *Id.*

96. *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1376 (Fed. Cir. 2015).

underlying phenomenon itself. Note though, that Lourie’s explanation is not accepted by all the Federal Circuit judges, which adds to § 101 uncertainty. Judge Reyna, who wrote the *Ariosa* opinion but dissented in *Illumina*, explicitly rejected adhering to Lourie’s characterizations.<sup>97</sup> This Essay agrees with Reyna’s line of thought—if the Federal Circuit is going to declare “diagnostic” methods ineligible but “treatment” or “preparation” methods eligible, it should do so at step two, not step one.

The confusion here can likely be attributed to a merging of the *Mayo/Alice* steps.<sup>98</sup> For example, in *Illumina*, the majority attempted to differentiate the case from *Ariosa* at step one by arguing that “the claimed methods *achieve* more than simply observing that fetal DNA is shorter than maternal DNA or detecting the presence of that phenomenon.”<sup>99</sup> This language focused on what the claims *achieved* and looked a lot like an analysis to determine if the claims “do more” (i.e., if they transformed the claims). The court simply seemed more impressed with the inventiveness of the *Illumina* patent than what was shown in *Ariosa*.

Indeed, this is not the only time the Federal Circuit appears to rely on “what more” the claims do to find direction to patentable subject matter at step one. In *Vanda Pharmaceuticals Inc. v. West-Ward Pharmaceuticals International Ltd.*, the Federal Circuit analyzed claims very similar to those found in *Mayo*.<sup>100</sup> Like the claims in *Mayo*, the claims in *Vanda* were for a method that started by administering a drug and then determining how a patient’s body had metabolized the drug.<sup>101</sup> The only difference between the claims in *Vanda* and *Mayo* was that the *Vanda* patent went a small step further than *Mayo* and proposed a specified dosage of drug to be administered in response to the correlation of metabolite observed.<sup>102</sup> This was enough for the court

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97. *Illumina*, 967 F.3d at 1330 (Reyna, J. dissenting) (“The asserted claims are directed to a natural phenomena . . .”).

98. The Federal Circuit has recognized this merging and overlap between the two steps, but its reasoning and articulation for how such overlap occurs is lackluster. *Caredx, Inc. v. Natera, Inc.*, 40 F.4th 1371, 1379 (Fed. Cir. 2022) (citing *Elec. Power Grp., LLC v. Alstom S.A.*, 830 F.3d 1350, 1353 (Fed. Cir. 2016)).

99. *Illumina*, 967 F.3d at 1326 (emphasis added).

100. *Vanda Pharms. Inc. v. West-Ward Pharms. Int’l Ltd.*, 887 F.3d 1117 (Fed. Cir. 2018).

101. *Id.* at 1121; *see also Mayo Collaborative Servs. v. Prometheus Lab’ys, Inc.*, 566 U.S. 66, 74–75 (2012).

102. *Vanda*, 887 F.3d at 1121.

to find the claims patent eligible.<sup>103</sup> The determination that the *Vanda* claims were directed to patent eligible subject matter was decided by relying on the fact that the claims did “more” and described treatment steps.<sup>104</sup>

It is difficult to fully comprehend how the court concluded that merely adding a suggested range of dosages to the claims changed their direction and satisfied finding validity at step one. This confusing standard of analysis can be seen in other cases finding validity at step one.<sup>105</sup> It is thus asserted that the state of the “directed to” step of the *Mayo/Alice* framework is uncertain and has led to a merging of step one and step two of the test.<sup>106</sup>

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103. *Id.* at 1136.

104. *Id.* at 1135.

105. See *Endo Pharms. Inc. v. Teva Pharms. USA, Inc.*, 919 F.3d 1347 (Fed. Cir. 2019) (finding validity at step one even though the claims did not go as far as *Vanda* and simply instructed an “increase” or “decrease” in the dosage after observing the correlation); *Nat. Alts. Int’l, Inc. v. Creative Compounds, LLC*, 918 F.3d 1338, 1343–44 (Fed. Cir. 2019) (finding claims that simply said to give the subject “an amount of [drug] . . . effective to increase [dipeptide molecule] synthesis in the human tissue” to be directed at patent eligible subject matter); *XY, LLC v. Trans Ova Genetics, LC*, 968 F.3d 1323 (Fed. Cir. 2020) (finding a claim using a well-known equation to separate X and Y carrying sperm from each other directed to patent eligible subject matter).

106. Additionally, the *Illumina* court did not have the foresight to examine the treatment claims in *In re Zunshine*, which highlighted an inconsistency in determining treatment claim eligibility. In 2020, Mr. Zunshine poked a hole in the court’s analyses of treatment claims when he contested a decision by the USPTO that his method for weight loss was ineligible. *In re Zunshine*, 816 F. App’x 477 (Fed. Cir. 2020). On its face (and simply put), *In re Zunshine* is a goofy case. Mr. Zunshine’s claimed method of weight loss involved a simple (but specific) process of cutting food intake by about one-third and following a plan of only eating at mealtimes or otherwise ingesting a glass of water first when hungry and then waiting ten to fifteen minutes, and, if still hungry, eating a snack that was determined by the subject’s BMI. *Id.* at 478. The court wholeheartedly rejected the claims at both steps of the *Mayo/Alice* test. *Id.* at 480. However, what is interesting is that at step one, the court stated the claims were directed at an abstract idea as they “amount[ed] to nothing more than reducing food intake to achieve weight loss and snacking to curb hunger.” *Id.* at 479. This Essay offers no opinion on if the court ultimately came to the correct conclusion in this case, but it does emphasize the inconsistency between *In re Zunshine* and a case like *Endo*, where the court held that responding to a viewed correlation by “increasing” or “decreasing” the dose given to the subject was eligible at step one. *Endo*, 919 F.3d at 1350–51. Mr. Zunshine also provided a method of performing a diagnostic (i.e., whether the subject was hungry at a specified time) and responding with a specified (albeit simple) treatment.

2. The Warning of Blurring § 101 with §§ 102 and 103 Has Created an Unforeseen Issue

In *Mayo*, the Supreme Court recognized that an inquiry into patent eligible subject matter and novelty or obviousness may overlap.<sup>107</sup> In doing so, the Court emphasized that “to shift the patent-eligibility inquiry entirely to these later sections risks creating significantly greater legal uncertainty . . . .”<sup>108</sup> The Court was not necessarily correct in its prediction. Indeed, there is a near certainty at step two for biotechnology patents: patent invalidation.

Recall that at step two of the *Mayo/Alice* test, the Supreme Court instructed the lower courts to look at the claims’ method steps separately and in their entirety.<sup>109</sup> The inventive concept that the courts are to seek cannot merely be a “well-understood, routine, conventional activit[y] previously known in the industry.”<sup>110</sup> It should also be recalled though, that the added step in the *Alice* case was the simple application of an equation to a “generic computer.”<sup>111</sup>

Although some biotechnology cases can be said to add this level of generality to their claims,<sup>112</sup> others likely do not. Take for example the claims in the patent at issue in *Athena Diagnostics, Inc. v. Mayo Collaborative Services*.<sup>113</sup> Acetylcholine receptor antibodies can indicate if someone has the disease myasthenia gravis (MG).<sup>114</sup> Up until the patent at issue, it was noted that only 80% of MG patients produced such antibodies; meaning that 20% of patients were going undiagnosed.<sup>115</sup> The inventors discovered that those 20% do produce MuSK antibodies though, and thus created a method of diagnosing virtually all those that have

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107. *Mayo Collaborative Servs. v. Prometheus Lab’ys, Inc.*, 566 U.S. 66, 90 (2012).

108. *Exergen Corp. v. Kaz USA, Inc.*, 725 F. App’x 959, 976 (Fed. Cir. 2018) (Hughes, J. dissenting) (citing *Mayo*, 566 U.S. at 90).

109. *Alice Corp. v. CLS Bank Int’l*, 573 U.S. 208, 217 (2014).

110. *Id.* at 225 (citing *Mayo*, 566 U.S. at 73).

111. *Id.*

112. *See e.g.*, *Genetic Techs. Ltd. v. Merial LLC*, 818 F.3d 1369 (Fed. Cir. 2016) (examining a claim of amplification of a particular gene using standard methods of amplification); *Cleveland Clinic Found. v. True Health Diagnostics, LLC*, 859 F.3d 1352 (Fed. Cir. 2017) (using standard methods to detect the enzyme MPO and then stating at what level the subject was more likely to be at risk for cardiac issues).

113. 915 F.3d 743 (Fed. Cir. 2019).

114. *Id.* at 747.

115. *Id.*

MG.<sup>116</sup> This was a great improvement from the previous methods.<sup>117</sup> Nonetheless, the court felt that it was applying known techniques in combination and thus not patentable.<sup>118</sup> This theory and application to MuSK had never been tried before and clearly had gone unconsidered by others in the field. But the court still found that it was just well-known steps in an order that was not substantially special.<sup>119</sup> The *Athena* case indicates what a high bar step two can be for inventors to overcome.

This “certainty” of patent invalidation at *Mayo/Alice* step two is not to say that there hasn’t been some inconsistency and confusion also created at this step. Compare the holding in *Athena*, with the holding in *Rapid Litigation Management Ltd. v. CellzDirect, Inc.*<sup>120</sup> In *CellzDirect*, the court examined claims that surrounded a method of freezing and thawing liver cells, called hepatocytes, for future use.<sup>121</sup> Although the court found the method eligible at step one of the *Mayo/Alice* analysis it still decided to perform a step two analysis to show that its holding was correct at either step.<sup>122</sup> The evidenced prior art methods involved freezing the cells one time for fear that more re-freezing could destroy the cells.<sup>123</sup> The new method simply inferred that such assumption was wrong and stated that the re-freezing could be done twice for better outcomes.<sup>124</sup> Thus the court felt that simply saying “repeat the well-known practice” was enough of an inventive concept to “do more.” Compare this holding to *Athena*, where the application of known steps to a new subject seemed to be significantly more advanced and unthought of, but not enough for eligibility.

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116. *Id.*

117. *Id.*

118. *Id.* at 751.

119. *Id.*

120. 827 F.3d 1042 (Fed. Cir. 2016).

121. *Id.* at 1045. Not only do hepatocytes help in “metabolism, detoxification, and protein synthesis” but they also help in producing bactericidal complement proteins that fight infection. Zhou Zhou, Ming-Jiang Xu & Bin Gao, *Hepatocytes: A Key Cell Type for Innate Immunity*, 13 CELLULAR & MOLECULAR IMMUNOLOGY 301, 301–02 (2016).

122. *CellzDirect*, 827 F.3d at 1050–51.

123. *Id.* at 1045.

124. *Id.*

### III. FOCUSING ON PREEMPTION AS THE UNDERLYING STANDARD FOR § 101 INQUIRIES

This Essay endorses Senator Tillis's proposed amendment and commends it for recognizing the issue in the *Mayo/Alice* framework as it pertains to examining novelty and obviousness in a § 101 analysis. Further, it suggests that the proposed amendment include language highlighting the importance of preemption.

The underlying preemption concern emphasized by the Supreme Court has been largely disregarded by the Federal Circuit.<sup>125</sup> As soon as a year after *Alice*, the Federal Circuit started to state that “[w]hile preemption may signal patent ineligible subject matter, the absence of complete preemption does not demonstrate patent eligibility.”<sup>126</sup> The only time preemption seems to be worth mentioning by the Federal Circuit is when the court rules that preemption does not apply to the case at hand.<sup>127</sup> Therefore, future legislation on § 101 should emphasize a concern about preemption and should put it at the forefront of the § 101 analysis.

Focusing on preemption will likely lead to a more understandable standard for cases involving a § 101 inquiry. This Essay shows how focusing on preemption could fix inconsistencies through separating the biotechnology cases into its own categories that are similar but different from Judge Lourie's. These categories include: (1) the natural thing itself; (2) methods to amplify or collect more of a natural thing; and (3) methods of comparison and response. These categories may not be exclusive,

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125. *See Alice Corp. v. CLS Bank Int'l*, 573 U.S. 208, 216 (2014) (“We have described the concern that drives this exclusionary principle as one of pre-emption.”).

126. *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1379 (Fed. Cir. 2015); *see also CellzDirect*, 827 F.3d at 1052 (stating the same); *Cleveland Clinic Found. v. True Health Diagnostics, LLC*, 859 F.3d 1352, 1363 (Fed. Cir. 2017) (same); *Roche Molecular Sys., Inc. v. Cepheid*, 905 F.3d 1363, 1374 (Fed. Cir. 2018) (same); *Athena Diagnostics, Inc. v. Mayo Collaborative Servs.*, 915 F.3d 743, 752 (Fed. Cir. 2019) (“Preemption is sufficient to render a claim ineligible under § 101, but it is not necessary.”).

127. *Vanda Pharms. Inc. v. West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1135 (Fed. Cir. 2018) (distinguishing from *Mayo*, saying that the claims directed at treatment do not “tie up the doctor's subsequent treatment decision.”); *Endo Pharms. Inc. v. Teva Pharms. USA, Inc.*, 919 F.3d 1347, 1354 (Fed. Cir. 2019) (“Nor is preemption a valid concern.”).

but generally fit the cases post-*Alice* and will provide a clearer standard going forward.<sup>128</sup>

#### A. COMMENDING SENATOR TILLIS'S AMENDMENT REMOVING A NOVELTY OR OBVIOUSNESS INQUIRY UNDER § 101

One of the major issues with the *Mayo/Alice* framework, and how the Federal Circuit has been applying it, is that it blurs the line of a § 101 inquiry into §§ 102 and 103 inquiries analyzing novelty and obviousness of an invention.<sup>129</sup> Senator Tillis's proposed legislation specifically calls for such an analysis to be abolished.<sup>130</sup> This Essay agrees with the proposition. This inquiry was happening at step two of the analysis, and as noted, of the fifteen cases analyzed, eight held the patent at issue failed step one of the test.<sup>131</sup> None of those eight cases went on to hold the patent at issue passed step two.<sup>132</sup> Doing away with the inquiry will further do away with subjectivity and the clearly high burden biotechnology inventions are being forced to endure.

#### B. PREEMPTIVE CATEGORIES

##### 1. The Natural Phenomenon Itself

These cases are largely self-explanatory and the easiest of the three categories to dismiss based on preemption. Because natural products cannot be patented, claims for them should be held invalid. This has largely been done by the Federal Circuit thus far. For example, here are three such cases that fit into this category: *In re Roslin Institute (Edinburgh)* (attempting to patent Dolly the sheep);<sup>133</sup> *In re BRCA1- and BRCA2-Based Hered-*

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128. It should be noted that in biotechnology cases, the underlying patent ineligible concept is usually a natural phenomenon or law as opposed to an abstract idea.

129. See *supra* Part II.B.2.

130. Patent Eligibility Restoration Act, S. 4734, 117th Cong. §§ 101(c)(1)(A)(ii), (iv) (2022).

131. *Ariosa*, 788 F.3d 1371; *Genetic Techs. Ltd. v. Merial LLC*, 818 F.3d 1369 (Fed. Cir. 2016); *Cleveland Clinic*, 859 F.3d 1352; *Roche*, 905 F.3d 1363; *Athena*, 915 F.3d 743; *Genetic Veterinary Scis., Inc. v. Laboklin GmbH & Co. KG*, 933 F.3d 1302 (Fed. Cir. 2019); *INO Therapeutics LLC v. Praxair Distrib. Inc.*, 782 F. App'x 1001 (Fed. Cir. 2019); *Caredx, Inc. v. Natera, Inc.*, 40 F.4th 1371 (Fed. Cir. 2022).

132. See *supra* Part II.B.2.

133. 750 F.3d 1333 (Fed. Cir. 2014).

*itary Cancer Test Patent Litigation* (attempting to patent a primer used for BRCA1 and BRCA2 polymerase);<sup>134</sup> and *Roche Molecular Systems, Inc. v. Cepheid* (attempting to patent a primer for a gene found in MTB bacteria).<sup>135</sup>

It should be noted that the latter two cases could arguably be patentable under *Myriad*. In that case, the Supreme Court invalidated a claim of the naturally occurring DNA because it was simply a reproduction of the DNA seen in nature.<sup>136</sup> Although, the Court expressed that if the claims were directed at a unique molecule that incorporated the DNA in a way that was not naturally occurring they could possibly be patentable.<sup>137</sup> This analysis is seen in *Roche*, where the Federal Circuit noted that adding a primer to a DNA sequence does incorporate a different end sequence than what is seen in the naturally occurring DNA—arguably making the claims in line with the *Myriad* standard, though, Roche eventually failed in its patent bid.<sup>138</sup> There is clearly some level of tension between these opinions. Ultimately, because all three of these cases involved an attempt at patenting a naturally occurring product, anyone attempting to work with those products for *any* future endeavor would be preempted from doing so. That makes the claims in all three of these cases unpatentable. Thus, a stronger emphasis on preemption in an amendment would instruct the court to continue to find claims like these invalid, but it would also likely overrule any doubt created by *Myriad*.

## 2. Methods that Amplify or Collect More of a Natural Phenomenon

Within the biotechnical field, there is often a desire to amplify or multiply a naturally occurring thing to create a larger sample that can be observed or tested. What needs to be determined in a § 101 case is if the claims are actually claiming a

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134. 774 F.3d 755 (Fed. Cir. 2014).

135. 905 F.3d 1363.

136. *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576, 590–91 (2013).

137. *Id.* at 592–93 (highlighting that the *Myriad* claims were directed to the underlying genetic information, not the unique severed molecule but seeming open to the unique molecule patentability with the caveat that it would be hard to enforce against “would-be infringers” should they change even just a few base pairs).

138. *Roche*, 905 F.3d at 1369 (“Specifically, Roche argues that the claimed primers have both a 3-prime end and a 3-prime hydroxyl group, while the naturally occurring bacterial MTB DNA contains neither of these.”).



method or if they are attempting to preempt others from using the natural thing itself. Within this category seems to be two subcategories, the first is pure amplification of the product. A great example of this comes in *Genetic Technologies Ltd v. Merial LLC*, where the claims simply said to amplify a certain region of DNA with a primer pair.<sup>139</sup> The other subcategory seems to be claims for sorting mechanisms to divide a sample to obtain the desired product found within the sample. Examples of this are seen in the *Illumina* case<sup>140</sup> and in *XY, LLC v. Trans Ova Genetics, LLC*, a case involving a method to sort X and Y carrying sperm.<sup>141</sup>

The Federal Circuit's conclusion in *Genetic Technologies* was that the patent was ineligible and the patents in *Illumina* and *XY, LLC* were eligible. A focus on preemption likely does not change the outcomes of these cases but it better articulates why these cases are different. In *Genetic Technologies* the claims were to simply amplify the product. This is likely something any scientist would want to do if they wanted to pursue study of the DNA sequence highlighted in the claims. Thus, in essence, the claims were preempting any possible work with the DNA sequence at issue for future inventors. There likely would be no substantive difference in the outcome were the patent to be granted for that DNA sequence itself. In contrast, the *Illumina* and *XY, LLC* inventions involved specific methods of sorting. These were not the only possibilities to sort and therefore they did not stop future inventors from sorting the DNA or sperm through different methods. Any sort of claim that simply says "amplify it" is putting a preemptive hold on the thing being amplified which is likely a natural phenomenon.<sup>142</sup>

For the most part, the Federal Circuit's decisions in this category largely match the outcomes a preemption-based test would have produced. But again, the main goal of § 101 reformation is not necessarily to change the outcomes of cases entirely, it is to

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139. 818 F.3d 1369, 1372 (Fed. Cir. 2016).

140. See *supra* notes 84–97 and accompanying text.

141. 968 F.3d 1323 (Fed. Cir. 2020).

142. See *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1373–74 (Fed. Cir. 2015) (“[M]ethod comprises amplifying a paternally inherited nucleic acid . . . .”); *Roche*, 905 F.3d at 1367 (“[S]ubjecting DNA from the [MTB] sample to polymerase chain reaction . . . .”); *Genetic Veterinary Scis. v. Laboklin GmbH & Co. KG*, 933 F.3d 1302, 1316 (Fed. Cir. 2019) (“The method according to claim 1, wherein the genotyping is achieved by real-time PCR . . . [or] utilizes a primer pair . . . .”).

better articulate how the similar cases can be distinguished and create clearer standards. By emphasizing a concern of preemption, inventors likely have a better understanding of what type of amplification can be patented.<sup>143</sup>

### 3. Methods of Comparison and Response to a Natural Law

The final category is the most difficult of the three. Unlike Judge Lourie's "method of treatment category" this category includes both methods of treatment as well as the diagnostic claims that involve a response (or lack thereof) to an observed natural law. Obviously, within the field of biotechnology, many inventions have to do with diagnostic and treatment. *Mayo* provides an excellent example for this.<sup>144</sup> The reason the *Mayo* claims were invalid under § 101 was because the claims simply stated a specified reading "indicated" a need for a response but did not necessarily tell the user how to respond.<sup>145</sup> In this way, the claims preempted anyone from responding to such observation without violating the patent. Another example of this is *Cleveland Clinic Foundation v. True Health Diagnostics LLC*.<sup>146</sup> There, the claims were for a medical professional to compare enzyme readings with a premade chart that displayed what levels of the enzyme correlated to increased risk of cardiac issues.<sup>147</sup> There was no described response to the readings, thus the methods preempted medical professionals from diagnosing and responding to the readings.

The best example of a response that would not preempt future remedy possibilities is shown in *Vanda*. *Vanda* is highly controversial but displays enough of a specific response that the court determined the claims in the patent at issue were valid.<sup>148</sup> The method claims instructed the physician to perform a diagnostic reading of what genotype the patient displayed and respond by administering specified dosage ranges of the treatment

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143. *PerkinElmer, Inc. v. Intema Ltd.* could also fit in this category. 496 F. App'x 65 (Fed. Cir. 2012). This is one of the cases that was decided between *Mayo* and *Alice* and had to do with a method for detecting risk of Down syndrome in unborn children. *Id.* at 66–67. The claims failed both step one and step two. *Id.* at 73.

144. *Mayo Collaborative Servs. v. Prometheus Lab'ys, Inc.*, 566 U.S. 66, 73 (2012).

145. *Id.* at 79.

146. 859 F.3d 1352 (Fed. Cir. 2017).

147. *Id.* at 1356–58.

148. *Vanda Pharms. Inc. v. West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117 (Fed. Cir. 2018).

medication.<sup>149</sup> Therefore, by reason of preemption, the claims were valid because future inventors could specify ranges that varied from what was suggested.

*Natural Alternatives International, Inc. v. Creative Compounds, LLC*<sup>150</sup> and *Endo Pharmaceuticals Inc. v. Teva Pharmaceuticals USA, Inc.*<sup>151</sup> are examples of where the court is applying a standard that deviates too far away from preemption principles. In both cases the methods simply stated the response was to increase or decrease the dosage of substance that was being given but were found eligible.<sup>152</sup> It must be generally accepted, though, that after taking a reading of a correlated level (i.e., observing the natural law) from a patient, a doctor is going to respond in one of three ways: either increase, decrease, or keep the same the dosage of the drug they are giving. This was likely the expected response in *Mayo*. By using such simple language with no specified dosage response, the claims in *Natural Alternatives* and *Endo* clearly tie up doctors' ability to respond to what they observe in a way that would not infringe the patent. Thus, the claims in *Natural Alternatives* and *Endo* created the same practical problems the claims in *Mayo* would have. In contrast, the claims in *Vanda* specified a range that provided *some* opportunity for doctors to vary from what was recommended by the patent and, in that way, did not preempt future study on response options.

The *Endo* court tried to differentiate itself from *Mayo* by stating (1) that the *Mayo* drug was not actually being used for treatment of a *particular disease* (i.e., it was only used to see metabolite breakdown), and (2) the administering step of the *Endo* patent occurred after observation of the correlation with a specified dose.<sup>153</sup> This reasoning is flawed on both grounds. First, there is no reason given for why the treatment of a specific disease matters. Both methods in *Mayo* and *Endo* attempted to tie up a *response* to the observed correlation. Even if the *Endo* claims were directed at the response using a single drug, they

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149. *Id.* at 1121–22.

150. 918 F.3d 1338 (Fed. Cir. 2019).

151. 919 F.3d 1347 (Fed. Cir. 2019).

152. *Id.* at 1351 (stating that a *lower* dosage should be given to patients based on the creatinine levels observed but not specifying what that lower dosage should be); *Nat. Alts.*, 918 F.3d at 1343 (emphasis in original) (“[P]roviding to the human subject an amount of an amino acid to blood or blood plasma *effective to increase beta-alanylhistidine dipeptide synthesis . . .*”).

153. *Endo*, 919 F.3d at 1350–51.

still tied up any response with that drug. Second, the court's statement in *Endo* that the response was with a specified drug amount like what was seen in *Vanda* was a lofty one. The *Endo* claims simply recommend a *lower* dosage to arrive at a desired correlation value.<sup>154</sup> In this way there really is no practical difference between *Endo*, *Mayo*, and *Cleveland Clinic* (the case observing MPO correlation to cardiac health issues). Therefore, it is likely that, under a strong preemption standard, the patents in *Natural Alternatives* and *Endo* would have been found to be invalid under § 101.<sup>155</sup>

By articulating that mere observation is not enough because of preemption principles, inventors will likely have a better understanding on what they need to do to qualify for a patent. However, those inventors need to provide a specific response to what they are observing.<sup>156</sup>

### CONCLUSION

For the patent system to have any real meaning, inventors need to know what innovation and invention will be eligible for patenting. Unfortunately, it is rarely doubted that the modern state of § 101 jurisprudence is in dismay and needs to be saved by either another ruling of the Supreme Court or legislation amending § 101. It seems the Court is going to leave it to the legislators, and because of Senator Tillis, there is a chance that such an amendment will happen.

As it pertains to biotechnology cases, the Federal Circuit has exemplified the issues with the Supreme Court's attempt to articulate a standard for patentable subject matter. To create a system with clearer standards for inventors and the lower courts, future legislation should do away with any sort of novelty

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154. *Id.* at 1351.

155. It should be highlighted that *Natural Alternatives* makes things even more confusing than *Endo*. There the court validated a product claim that basically secured the use of beta-alanine between 0.4 and 16 grams. *Natural Alternatives*, 918 F.3d at 1348. The opinion was written by Judge Moore who—after observing these cases—is concluded to be by far the most favorable circuit judge for broad patentability under § 101.

156. Another case this Essay deems to have been decided wrongly is *Athena Diagnostics, Inc. v. Mayo Collaborative Services*, 915 F.3d 743 (Fed. Cir. 2019). This is the case regarding the detection of MuSK proteins. The preemptive nature here was likely minimal because like the *CellzDirect* case, there were other methods of diagnosis and the one created by the inventors was not preempting others from using the prior methods.

or obviousness analysis under § 101. More importantly, the legislation should emphasize the importance of preemption in the § 101 inquiry. Senator Tillis's proposed amendment does the former but says nothing about the latter. This Essay encourages added language on this "preemption" standard. Doing so will reconcile some confusing past cases and, more importantly, create a much clearer standard going forward for courts and inventors.