NOTE

UNDUE COMPUTATIONAL EXPERIMENTATION: CAN *IN SILICO* EXPERIMENTS ALLOW GENUS CLAIMS TO SURVIVE?

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U.S. courts have, time and again, struck down genus claims for undue experimentation. The most recent blow came last year in Amgen v. Sanofi, when the Supreme Court affirmed the lower court's ruling that Amgen's patent on antibodies with a specific target was invalid for lack of enablement. In that ruling, the Court invoked the rule that "the more one claims, the more one must enable." Meanwhile, science is being revolutionized by computational experimentation, especially in the fields of medicine, biotechnology, nanotechnology, and chemistry. These changes are enabling research at a scale hitherto thought impossible. This Note analyzes the standard of patentability in the context of computational experimentation, with an emphasis on computer-aided drug design. With a focus on Amgen and the Wands factors, this Note will argue that computational experimentation is enabling of genus claims, especially in the area of chemistry and pharmaceutical research.

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INTRODUCTION

On December 13, 2019, Juno Therapeutics and the Sloan Kettering Institute for Cancer Research received a decision in their patent infringement case against Kite Pharma regarding Kite's drug, Yescarta.[1] The jury awarded the plaintiffs over $778 million in damages.[2] Post-trial motions would raise this award to over $1.1 billion.[3] And yet Juno would not receive this award. Why? Put simply, the court ruled that Juno's patent was invalid as it was too broad.[4]

This trail is well-trod. In 1854, the Supreme Court found that Samuel Morse's claim for using electromagnetism to write at a distance was too broad.[5] In 1895, the same fate befell William Sawyer and Albon Man's claim for fibrous or textile incandescent materials.[6] And again, in 1928, to Perkins Glue Company's claim for starch glue combined with water.[7] Most recently, Amgen's claim to a class of antibodies fell upon the same sword.[8]

All these claims share a common feature: rather than claiming a specific structure of invention, they claim a class of structures that follow a basic idea. They are, in other words, "genus claims." These genus claims are particularly appealing to modern patent lawyers in the chemical arts, as they can assure that no one can copy a basic idea and bypass patent infringement by changing a small detail.[9] Nonetheless, courts constantly strike down these claims due to a need for undue experimentation.[10]

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1 *Sloan Kettering and Juno Therapeutics win over $1.1 billion after jury verdict and post-trial motions in patent dispute with Kite Pharma/Gilead involving CAR-T therapy*, JONES DAY, https://www.jonesday.com/en/practices/experience/2020/04/sloan-kettering-and-juno-therapeutics-win-752-mill (last visited Dec. 6, 2023) [https://perma.cc/LF9D-9TP5].

2 *Id.*

3 *Id.*

4 *See* Juno Therapeutics, Inc. v. Kite Pharma, Inc., 10 F.4th 1330, 1336 (Fed. Cir. 2021), *cert. denied*, 143 S. Ct. 402 (2022). The court goes on to detail how the claims at issue fail to meet the specification requirements of 35 U.S.C. § 112(a). *Id.* at 1336–40.

5 O'Reilly v. Morse, 56 U.S. 62, 113 (1854).

6 The Incandescent Lamp Patent, 159 U.S. 465, 475–76 (1895).

7 Holland Furniture Co. v. Perkins Glue Co., 277 U.S. 245, 256–58 (1928).

8 Amgen Inc. v. Sanofi, 598 U.S. 594, 614 (2023).

9 Dmitry Karshtedt, Mark A. Lemley, & Sean B. Seymore, *The Death of the Genus Claim*, 35 HARV. J.L. & TECH. 1, 3 (2021).

10 *See, e.g.*, *The Incandescent Lamp Patent*, 159 U.S. at 475–77; *Amgen*, 598 U.S. at 614.

Meanwhile, science marches on. In the past few decades, computational experimentation has substantially changed the playing field for medicine, biotechnology, nanotechnology, and chemistry.[11] In just three years, Google's AlphaFold has recreated the structure of over 200 million proteins.[12] This rapid progress far eclipses the 219,869 protein structures reported to the Protein Data Bank, the foremost repository of protein structures, in fifty years.[13] This revolution was recently honored with the 2024 Nobel Prize in Chemistry.[14] Similarly, the option of "virtual screening" of drugs has enhanced the rate of screening drug candidates. Labs employing this method have been able to computationally screen upwards of half a million drug candidates against disease targets.[15] These effects are complementary, as many virtual screening methods require a protein target with a known and accurate structure.[16]

In light of the ongoing revolution of computational experimentation and its impact on the demands of engineers and research, we must re-evaluate what undue experimentation looks like, and whether genus claims or similar broad-reaching claims may be enabled as a result. In this note, I will argue as much, with a particular focus on the Court's recent decision in *Amgen v. Sanofi* and the Federal Circuit's enumerated *Wands*

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11 Hereinafter, these fields, different as they may be, will be grouped into "chemistry."

12 *AlphaFold Protein Structure Database*, EUROPEAN MOLECULAR BIOLOGY LABORATORY—EUROPEAN BIOINFORMATICS INSTITUTE, https://alphafold.ebi.ac.uk/ (last visited May 15, 2024) [https://perma.cc/474F-CZ9T].

13 *PDB Statistics: Overall Growth of Released Structures Per Year*, RESEARCH COLLABORATORY FOR STRUCTURAL BIOINFORMATICS, https://www.rcsb.org/stats/growth/growth-released-structures (last visited May 15, 2024) [https://perma.cc/V24T-M3H5].

14 *Press Release: The Nobel Prize in Chemistry 2024*, NOBEL PRIZE OUTREACH AB 2024, https://www.nobelprize.org/prizes/chemistry/2024/press-release/ (last visited Oct. 18, 2024) [https://perma.cc/WCK4-L3RR].

15 Eric R. Hantz & Steffen Lindert, *Actives-Based Receptor Selection Strongly Increases the Success Rate in Structure-Based Drug Design and Leads to Identification of 22 Potent Cancer Inhibitors*, 62 J. CHEM. INFO. & MODELING 5675, 5677–78 (2022).

16 *See* SM Bargeen Alam Turzo, Eric R. Hantz, & Steffen Lindert, *Applications of Machine Learning in Computer–Aided Drug Discovery*, Q. REVS. BIOPHYSICS DISCOVERY, Sept. 2022, at 1 (describing structure-based drug design as a subfield of computer-aided drug design which requires the three-dimensional structure of targets).

factors. In Part I,[17] I will discuss U.S. patent law with a focus on the standard of undue experimentation. In Part II,[18] I will discuss the status of modern computational experimentation and detail some of the revolutions therein. In Part III,[19] I will apply the court's prior decisions and argue that computational experimentation is substantially more enabling than traditional "benchtop" experimentation. Finally, in Part IV,[20] I will discuss the possible issues that this line of argument can raise with obviousness issues and ways to circumvent these issues, before concluding[21] with a brief look at the wider implications of undue experimentation law and genus claims.

I
U.S. PATENT LAW

In the United States, patent law allows an inventor to patent "anything under the sun made by man."[22] Such patents grant the owner the exclusive right to make commercial use of the claimed invention for a number of years.[23] Though there is a vast body of literature regarding U.S. patent law, four statutes set out the limitations of patentable materials: 35 U.S.C. §§ 101, 102, 103, and 112. Together, these define the five requirements of patents: utility,[24] patentable subject matter,[25] novelty,[26] non-obviousness,[27] and written specification.[28]

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17 *See* Part I, *infra*.

18 *See* Part II, *infra*.

19 *See* Part III, *infra*.

20 *See* Part IV, *infra*.

21 *See* Conclusion, *infra*.

22 Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980) (citing S. REP. NO. 1979, at 5 (1952); H. R. REP. NO. 1923, at 6 (1952)). However, by the time that the Court made this statement, they had already placed limits on things made by man that qualified as patentable subject matter. *See, e.g.*, Parker v. Flook, 437 U.S. 584, 594–95 (1978) (rejecting a patent for a novel method of updating alarm limits on subject matter grounds).

23 STAFF OF SUBCOMM. ON PATS., TRADEMARKS, & COPYRIGHTS OF THE S. COMM. ON THE JUDICIARY, 85TH CONG., AN ECONOMIC REVIEW OF THE PATENT SYSTEM 1 (Comm. Print 1958).

24 35 U.S.C. § 101.

25 *Id.*

26 35 U.S.C. § 102.

27 35 U.S.C. § 103.

28 35 U.S.C. § 112.

The utility requirement for a U.S. patent is very forgiving, only requiring that the invention have a specific benefit[29] and not be "frivolous or injurious to the well-being, good policy, or sound morals of society."[30] The limitation on patentable subject matter, set out in the same phrase as the utility requirement,[31] limits inventors to obtaining patent rights on processes, machines, manufactures, or compositions of matter, or improvements thereof.[32] Novelty, discussed in the immediately subsequent section,[33] bars patenting inventions that are already available in the public domain.[34] These works available in the public domain are commonly known as "prior art."[35]

The bar on obviousness extends the requirement of novelty to also include any non-published but obvious inventions. It requires that a person having ordinary skill in the art (POSITA) would not be able to combine prior art to obtain every limitation to a patent claim[36] or otherwise would not think to do so.[37] The Court has given three factual inquiries to consider to determine obviousness: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; and (3) the level of ordinary skill in the pertinent art.[38]

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29 Brenner v. Manson, 383 U.S. 519, 534–35 (1966). The benefit must be known at the time of patenting and cannot merely be as an object of use-testing. *Id.* at 535.

30 Lowell v. Lewis, 15 F. Cas. 1018, 1019 (C.C.D. Mass. 1817).

31 35 U.S.C. § 101 ("any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof").

32 *Id.* The Court has consistently stated that inventors can only patent things made by man; laws of nature, natural phenomena, and abstract ideas are manifestations of nature and cannot be owned. *See, e.g.*, Mayo Collaborative Servs. v. Prometheus Laby's., Inc., 566 U.S. 66, 70–71 (2012). This is most commonly raised as an issue for process patents. *Compare* Diamond v. Diehr, 450 U.S. 175, 192–93 (1981) (approving a process patent for producing rubber products using a mathematical formula), *with* Parker v. Flook, 437 U.S. 584, 594–95 (1978) (rejecting a process patent on updating alarm limits using a mathematical formula). The Court has given some useful instruction on this topic but has rejected a hard-and-fast test. *See, e.g.*, *Mayo*, 566 U.S. at 80–92.

33 35 U.S.C. § 102.

34 *In re* Hall, 781 F.2d 897, 898 (Fed. Cir. 1986).

35 35 U.S.C. § 102 details the requirements to be considered "prior art."

36 *Cf.* United States v. Adams, 383 U.S. 39, 51 (1966) (directly addressing the presence of every limitation in the claim, though later finding the patent non-obvious on other grounds).

37 *Id.* at 51–52.

38 KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 406 (2007) (quoting Graham v. John Deere Co., 383 U.S. 1, 17–18 (1966)). The Patent and Trademark

While considering obviousness, the breadth of prior art considered does not stretch as far as for novelty. Rather, prior art is only taken into consideration if it is analogous—that is, if it is from the same field as the invention or if it is "reasonably pertinent to the particular problem with which the inventor is involved."[39] The Court has also recognized several secondary considerations to defeat a challenge of obviousness, such as commercial success, long felt but unsolved needs, or failure of others.[40]

Section 112 introduces two more requirements, written description and enablement, often combined into "written specification" when listing the requirements for patentability.[41] Both of these may be considered a demand on the description of the invention given in the patent. The written description requirement states that a patent must allow a POSITA to clearly know the bounds of the inventor's claim.[42] Enablement, in contrast, requires that the patent applicant "enable any person skilled in the art . . . to make and use the [invention], and . . . set forth

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Office has further detailed several rationales for a finding of obviousness, including:

> (A) Combining prior art elements according to known methods to yield predictable results;
> (B) Simple substitution of one known element for another to obtain predictable results;
> (C) Use of known technique to improve similar devices (methods, or products) in the same way;
> (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;
> (E) "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;
> (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;
> (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

United States Patent and Trademark Office, MANUAL OF PATENT EXAMINING PROCEDURE § 2141.III (9th ed., rev. July 2022) [hereinafter "MPEP"].

39 *In re* Clay, 966 F.2d 656, 658–69 (Fed. Cir. 1992).

40 *Graham*, 383 U.S. at 17–18.

41 35 U.S.C. § 112.

42 Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (citing Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563 (Fed. Cir. 1991)). The written description requirement is also thought of as conveying to a POSITA that the inventor is in possession of the claimed subject matter. *Id.*

the best mode contemplated by the inventor or joint inventor of carrying out the invention."[43]

Though it does not appear in the statute, it is also well established that the patent must sufficiently enable a POSITA to make and use the invention *without undue experimentation*.[44] The key word in this is "undue"—"a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed."[45] The Court of Appeals for the Federal Circuit has given eight factors that are to be considered when determining whether experimentation is "undue," known collectively as the *Wands* factors:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.[46]

Enablement is a common route for courts to defeat genus claims.[47] A genus claim is a broad claim for a group of structurally related products that all follow the basic idea of the invention[48]—for example, a claim to "the use of . . . electromagnetism . . . for marking or printing intelligible characters, signs, or letters, at any distances."[49] These claims are

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43 35 U.S.C. § 112(a). However, the "best mode" requirement is less enforced as it may not be raised as grounds for cancellation or invalidity in an infringement suit. 35 U.S.C. § 282(b)(3)(A).

44 *In re* Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

45 *Id.* (quoting *Ex parte* Jackson, No. 463-26, 217 U.S.P.Q. 804, 807 (B.P.A.I. Nov. 12, 1982)).

46 *Id.* Though the Supreme Court has never discussed the *Wands* factors, they continue to be well-cited in articles, treatises, Supreme Court briefs, and federal cases. *See, e.g.*, Karshtedt, Lemley, & Seymore, *supra* note 9, at 8–9 (article); 3 DONALD S. CHISUM, CHISUM ON PATENTS § 7.03 (2023) (treatise); Brief for the American Intellectual Property Law Association as Amicus Curiae Suggesting Affirmance at 12–13, Amgen Inc. v. Sanofi, 598 U.S. 594 (2023) (No. 21-757) (brief); Medytox, Inc. v. Galderma S.A., 71 F.4th 990, 996 n. 5 (Fed. Cir. 2023) (case).

47 *See, e.g.*, The Incandescent Lamp Patent, 159 U.S. 465, 475–77 (1895); *Amgen*, 598 U.S. at 614.

48 Karshtedt, Lemley, & Seymore, *supra* note 9, at 3.

49 O'Reilly v. Morse, 56 U.S. 62, 112 (1854). The Court in this case cut to the heart of what made this a genus claim and what made such a claim problematic:

> If this claim can be maintained, it matters not by what process or machinery the result is accomplished. For aught that we now know some future

particularly common in the pharmaceutical, biotechnology, and chemical industries.[50] However, many of these claims do not survive when challenged.[51] Of those that do, most are either claims to a relatively small genus or claims to a genus that was well-known at the time of issue.[52]

It is enlightening to observe the Supreme Court's most recent brush with genus claims and enablement: *Amgen v. Sanofi*.[53] Across two patents, Amgen claimed "the entire genus of antibodies that bind to specific amino acid residues on PCSK9 and block PCSK9 from binding to LDL-Rs [(low density lipoprotein receptors)]," which would be used to treat high cholesterol.[54] As part of its patent submission, Amgen described twenty-six of the antibodies in the genus and provided a three-dimensional structure of two antibodies.[55] Beyond that, Amgen only provided two forms of enablement. First was a trial-and-error method known as the "roadmap," which involved generating sets of varying antibodies and testing for binding to PCSK9 and blocking of binding to LDL-Rs.[56] Second was a method called "conservative substitution," which involved starting with a known functional antibody and replacing parts of the antibody with similar parts, then testing to see if this antibody also functions as intended.[57]

The Court dismissed both of these tactics as "little more than two research assignments."[58] They further detailed that, though Amgen may have technically described how to arrive at all functional antibodies, Amgen's "roadmap" and "conservative

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> inventor, in the onward march of science, may discover a mode of writing or printing at a distance by means of the electric or galvanic current, without using any part of the process or combination set forth in the plaintiff's specification. His invention may be less complicated—less liable to get out of order—less expensive in construction, and in its operation. But yet if it is covered by this patent the inventor could not use it, nor the public have the benefit of it without the permission of this patentee.

Id. at 113.

50 Karshtedt, Lemley, & Seymore, *supra* note 9, at 3.

51 *See* Shahrokh Falati, *A Singular Disclosure Requirement is Necessary for Patent Law*, 24 COLUM. SCI. & TECH. L. REV. 249, 251 (2023).

52 Karshtedt, Lemley, & Seymore, *supra* note 9, at 49–50. *But see id.* at 46–49 (discussing the set of genus claims that survived the "now obsolete" proceeding of interference).

53 Amgen Inc. v. Sanofi, 598 U.S. 594 (2023).

54 Amgen Inc. v. Sanofi, 872 F.3d 1367, 1372 (Fed. Cir. 2017).

55 *Amgen*, 598 U.S. at 602–03.

56 *Id.*

57 *Id.*

58 *Id.* at 1256.

substitution" methods do not enable a POSITA sufficiently to obtain a patent over the entire genus.[59] The Court leaves a few helpful remarks regarding what may suffice to support a genus claim. First, a broad note that "[t]he more one claims, the more one must enable."[60] Second, a comment that an example may suffice for a genus claim if the specification also details a general quality to all members of the genus that gives it "a peculiar fitness for the particular purpose."[61] Third, and most remarkably, they allow that the "roadmap" or "conservative solution" may suffice to enable other claims, especially if they identify a "quality common to every functional embodiment."[62]

II
Computational Experimentation and Drug Discovery

In 1965, Gordon Moore, co-founder of Intel, observed that the number of transistors on a computer chip—and thus the computational power of computers—doubles roughly every year, and predicted that the trend would hold for at least 10 years.[63] His observation, now called "Moore's law," has held true for more than 50 years.[64] This trend has allowed for much of the technology used on a day-to-day basis, including smartphones, laptops, and GPS.[65] It has also led to the creation of artificial intelligence, deep neural nets, and other forms of

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59 Notably, the Court points out that the "roadmap" method was Amgen's own method for developing antibodies. *Id.* It seems difficult to argue that these methods were enabling for a POSITA to develop the antibodies revealed in the patent. Further, though it was not discussed, there is no indication that these antibodies were especially susceptible to the "roadmap," meaning that this method would be equally enabling for any set of twenty-six antibodies. And, given that it was enabling for any antibody, it should therefore be enabling for all antibodies. Nonetheless, the Court found the "roadmap" wanting for enablement.

60 *Id.* at 1254.

61 *Id.* (quoting The Incandescent Lamp Patent, 159 U.S. 465, 475 (1895)).

62 *Id.* at 1256.

63 Gordon E. Moore, *Cramming More Components onto Integrated Circuits*, 86 Proc. IEEE 82, 83 (1998). Moore later noted that the trend is actually closer to doubling every two years. *Moore's Law*, Intel (Sept. 18, 2023), https://www.intel.com/content/www/us/en/newsroom/resources/moores-law.html [https://perma.cc/6YRX-2GHP].

64 Max Roser, Hannah Ritchie, & Edouard Mathieu, *What is Moore's Law?*, Our World in Data (Mar. 28, 2023), https://ourworldindata.org/moores-law [https://perma.cc/TU89-SYVT].

65 David Rotman, *We're Not Prepared for the End of Moore's Law*, MIT Tech. Rev. (Feb. 24, 2020), https://www.technologyreview.com/2020/02/24/905789/were-not-prepared-for-the-end-of-moores-law/ [https://perma.cc/MR8V-4A45].

machine learning,[66] enabling the development of software like ChatGPT[67] and TensorFlow.[68]

Almost sixty years after Moore's observation, the Nobel Prize in Chemistry would be awarded to two people for harnessing the exponential increase in computational power. Demis Hassabis and John Jumper were awarded the 2024 Nobel Prize in Chemistry for their work on AlphaFold2,[69] a deep learning software that predicts the three-dimensional structure of proteins.[70] Along with the release of the AlphaFold software, Google released a database of over 350,000 protein structures.[71] This database has since grown to over 200 million highly-accurate structures,[72] far larger than the 213 thousand traditionally-obtained structures available on the Protein Data Bank.[73] Among the structures in AlphaFold's database is the entirety of the human proteome, the complete set of proteins expressed by humans.[74] Researchers have already used this

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66 A very brief overview of machine learning may prove valuable:

> Machine learning is the technique that improves system performance by learning from experience via computational methods. In computer systems, experience exists in the form of data, and the main task of machine learning is to develop learning algorithms that build models from data. By feeding the learning algorithm with experience data, we obtain a model that can make predictions . . . on new observations . . . . If we consider computer science as the subject of algorithms, then machine learning is the subject of learning algorithms.

ZHI-HUA ZHOU, MACHINE LEARNING 2 (Shaowu Liu trans., Springer Nature Singapore Pte Ltd. 2021) (2016). *See generally id.* ch. 1. Modern machine learning is performed with massive training data sets in order to obtain very accurate results. Much of modern machine learning is performed through neural networks. *See generally* BERNHARD MEHLIG, MACHINE LEARNING WITH NEURAL NETWORKS ch. 1 (2021).

67 *Introducing ChatGPT*, OPENAI (Nov. 30, 2022), https://openai.com/blog/chatgpt [https://perma.cc/62H4-ZCTW].

68 TENSORFLOW, https://www.tensorflow.org/ (last visited Dec. 8, 2021) [https://perma.cc/9SD7-W9L4].

69 *Press Release: The Nobel Prize in Chemistry 2024*, *supra* note 14.

70 John Jumper et al., *Highly Accurate Protein Structure Prediction with AlphaFold*, 596 NATURE 583, 583 (2021). The knowledge of a protein's three-dimensional structure is especially relevant to the issue of drug design and discovery in order to design activators and inhibitors. JOHN R. GUNN, *Computational Protein Folding*, *in* HIGH PERFORMANCE COMPUTING SYSTEMS & APPLICATIONS 333, 334 (Jonathan Schaeffer ed., 1998).

71 *AlphaFold*, GOOGLE DEEPMIND, https://deepmind.google/technologies/alphafold/ (last visited Dec. 7, 2023) [https://perma.cc/MT76-VDRQ].

72 *AlphaFold Protein Structure Database*, *supra* note 12.

73 *PDB Statistics*, *supra* note 13.

74 Jumper, *supra* note 70, at 588.

to better understand antibiotic resistance and create images of enzymes that can decompose plastic.[75] Other groups have noted the widely varied areas of application for AlphaFold, including structural biology, drug discovery, protein design and function prediction, protein target prediction, and protein-protein interaction prediction.[76]

This increase in computational power is not limited to AlphaFold. Methods such as computational chemistry,[77] computer-aided drug discovery (CADD),[78] protein folding,[79] and nanomaterial rational design[80] allow scientists to perform *in silico*[81] experiments which are far faster and less expensive than previous experimental methods. Turzo, Hantz, and Lindert discuss around twenty different methods of using machine learning for design of drug candidates, all published in the past decade.[82] Other authors have discussed the use of machine

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75 *See Press Release: The Nobel Prize in Chemistry 2024*, *supra* note 14.

76 Zhenyu Yang, Xiaoxi Zeng, Yi Zhao, & Runsheng Chen, *AlphaFold2 and its Applications in the Fields of Biology and Medicine*, 8 SIGNAL TRANSDUCTION & TARGETED THERAPY 1, 5–9 (2023), https://doi.org/10.1038/s41392-023-01381-z [https://perma.cc/SGE8-WDMW].

77 *See* generally ERROL G. LEWARS, COMPUTATIONAL CHEMISTRY: INTRODUCTION TO THE THEORY AND APPLICATIONS OF MOLECULAR AND QUANTUM MECHANICS 1–6 (3d ed. 2016) for an overview of the methods and capabilities of computational chemistry. The remainder of the book is an excellent investigation into the topic for those with sufficient chemical background.

78 Sumudu P. Leelananda & Steffen Lindert, *Computational Methods in Drug Discovery*, 12 BEILSTEIN J. ORG. CHEM 2694, 2695 (2016) (describing the use of CADD tools to identify lead drug molecules for testing, predict effectiveness and side effects, and assist in improving bioavailability of drug molecules).

79 GUNN, *supra* note 70, at 334 (describing the use of computer simulations to determine a protein conformation with minimal free energy).

80 Ryan L. Marson, Trung Dac Nguyen, & Sharon C. Glotzer, *Rational Design of Nanomaterials from Assembly and Reconfigurability of Polymer-Tethered Nanoparticles*, 5 MATERIALS RSCH. SOC'Y COMMC'NS. 397, 397 (2015) (describing the use of computational technologies to identify target nanostructures, candidate-building blocks, and efficient assembly pathways in order to design nanomaterials).

81 "*In silico*" loosely means "in computer" and is used to denote experimentation done purely with computer software. *See* S Ekins, J Mestres, & B Testa, *In Silico Pharmacology for Drug Discovery: Methods for Virtual Ligand Screening and Profiling*, 152 BRIT. J. PHARMACOLOGY 9, 9 (2007). It is used to contrast "*in vivo*," meaning "in life" and referring to experiments on living beings, and "*in vitro*," meaning "in glass" and referring to experiments in an artificial environment.

82 Turzo, Hantz, & Lindert, *supra* note 16, at 1–12.

learning in later phases of drug design, such as absorption,[83] metabolism,[84] and efficacy studies.[85]

These methods pay dividends. A review by Ekins, Mestres, and Testa notes no fewer than eighty papers where *in silico* experimentation was used to discover a potential drug candidate.[86] More recently, Turzo, Hantz, and Lindert reported on fifteen papers where CADD has been used to advance research in disease treatment.[87] As one example of many, Hantz and Lindert used CADD to scan over 500,000 potential drug compounds across five cancer-related target systems.[88] CADD reduced the pool of potential drug compounds to 250 potential cancer target inhibitors, of which subsequent high-throughput benchtop experiments identified twenty-two cancer target inhibitors.[89] For their most successful drug target, Colony Stimulating Factor 1 Receptor (CSF1R), Hantz and Lindert found fifty candidate molecules through CADD and confirmed twelve through benchtop experiments.[90]

III
Undue Experimentation

In *Incandescent Lamp Patent*, the Court made some to-do about Edison's experimental process: he and his assistants spent several months testing different species of vegetable growth; initial tests provided only three successful runs, one of which was unobtainable in sufficient quantities; for the remaining two, he was unable to slice the filament thin enough without damaging the integrity of the material; after that failure

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83 *See generally* Moonshik Shin, Donjin Jang, Hojung Nam, Kwang Hyung Lee, & Doheon Lee, *Predicting the Absorption Potential of Chemical Compounds Through a Deep Learning Approach*, 15 IEEE/ACM Transactions on Computational Biology and Bioinformatics 432 (2018).

84 *See* Disha Wang et al., *Deep Learning Based Drug Metabolites Prediction*, 10 Frontiers in Pharmacology 1, 4 (2020), https://doi.org/10.3389/fphar.2019.01586 [https://perma.cc/R6GL-8A66].

85 *See* Eugine Lin et al., *A Deep Learning Approach for Predicting Antidepressant Response in Major Depression Using Clinical and Genetic Biomarkers*, 9 Frontiers in Psychiatry, 1, 7 (2018), https://doi.org/10.3389/fpsyt.2018.00290 [https://perma.cc/V7TK-8TF6].

86 *See* S Ekins, J Mestres, & B Testa, *In Silico Pharmacology for Drug Discovery: Applications to Targets and Beyond*, 152 Brit. J. Pharmacology 21, 23 tbl.1 (2007) (discussing pharmacology targets where computational methods have been used to discover new molecules with binding affinity).

87 *See* Turzo, Hantz, & Lindert, *supra* note 16, at 1.

88 Hantz & Lindert, *supra* note 15, at 5677–78.

89 *Id.* at 5678–79.

90 *Id.* at 5682.

drove him nearly hopeless, he happened upon a more adequate bamboo material; he had to send a messenger to various parts of Japan and China to acquire sufficient variety of bamboo for testing; and even then, he was unable to find a common quality to bamboo that made it good as a filament.[91] To some extent, the Court was obliged to comment on this. They were, after all, attempting to argue that Sawyer and Man required too much experimentation to determine which fibrous or textile materials were adapted to the purpose of an incandescent conductor. Edison's painstaking experimentation was almost custom-fit to the Court's argument.

But what happens when Edison no longer needs to spend months on an ultimately doomed process of testing fibrous materials? When he doesn't need to send messengers across the globe to get testing materials? What happens when a scientist is able to choose a disease target, click a few buttons, and discover a class of drugs that are functional against the disease target?[92] At some point, the experimentation must no longer be undue, for it nearly ceases to be experimentation.

A. *Amgen* and the Hantz/Lindert Hypothetical

How would the Supreme Court react to these questions? Based on their recent ruling in *Amgen*, the answer is not particularly clear.

Let's properly construct the hypothetical. Hantz and Lindert conclude their experimentation on CSF1R, a protein associated with leukemia.[93] They've computationally tested every known drug-like molecule in one of the foremost small-molecule databanks, and found fifty candidates for inhibition of CSF1R. Subsequent benchtop testing confirmed twelve candidates.

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91 The Incandescent Lamp Patent, 159 U.S. 465, 472–74 (1895).

92 To be clear, I do not suggest that science is currently at this point. For one, the multifarious softwares used for CADD require more input than "click[ing] a few buttons." However, as interfaces and automation increase for this software, the process will become simpler for the end user. More importantly, current CADD should be followed up by benchtop experiments. Nonetheless, as CADD software becomes more accurate, the benchtop confirmation will be more redundant, and even now, a reduction from the entirety of described drug-like molecules to some 250 substantially reduces the amount of experimentation. *See* Hantz & Lindert, *supra* note 15, at 5677–78 (reducing the number of suspect drugs from the entirety of the ChemBridge EXPRESS-Pick Collection plus stereoisomers and enantiomers to 250).

93 Kristine Yttersian Sletta, Oriol Castells, & Bjørn Tore Gjertsen, *Colony Stimulating Factor 1 Receptor in Acute Myeloid Leukemia*, 11 FRONTIERS IN ONCOLOGY 1, 6 (2021), https://doi.org/10.3389/fonc.2021.654817 [https://perma.cc/EK9N-5QGQ].

They meet with a lawyer, confirm that there are no novelty or obviousness issues, and submit a patent. In the patent, they disclose their entire process and all twelve confirmed inhibitors but claim all small-molecule inhibitors of CSF1R. The claim is subsequently challenged on enablement grounds due to undue experimentation.

Structurally, this case is very similar to *Amgen*. The patentee claimed a class of drug that binds to a target. In their specification, in form of enablement, they provided their own method of research, which was to run a large group of candidates through testing and confirm which ones succeed. On its face, Hantz and Lindert are no more enabling than Amgen, and there is no general quality common to all functional embodiments. This patent ought to be dead in the water.

And yet, Hantz and Lindert differ from Amgen in key ways. First, in a pure sense of time taken to confirm a candidate, Hantz and Lindert require far less experimentation than Amgen. 99.99% of candidates will not see a benchtop with Hantz and Lindert's method, while every candidate will need a benchtop test under Amgen's instructions.[94] This certainly works in the favor of Hantz and Lindert.[95]

More significantly, Hantz and Lindert have some colorable claim that they have discovered and disclosed the entirety of their claim. They swept the entire breadth of a database of small molecules. They disclosed every viable candidate they found. Amgen did neither of these.[96] Certainly, some viable inhibitor may have failed the computational step or may have not been included in the database.[97] But "a considerable amount of experimentation is permissible" in this situation of routine testing.[98] And should a small molecule be discovered which

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94 Computational testing is not only faster to run than traditional benchtop testing, but far more computational tests can be run in parallel by a single lab hand than benchtop tests.

95 *See* White Consol. Indus., Inc. v. Vega Servo-Control, Inc., 713 F.2d 788, 791 (Fed. Cir. 1983) (using time required to practice as a factor for undue experimentation). In this discussion, we ignore the difference in experimentation between small molecules and antibodies. This is done at some peril—antibody synthesis is rather standardized, while small-molecule synthesis may be much faster or much more difficult than antibodies.

96 *See* Petition for Writ of Certiorari at 7–9, Amgen Inc. v. Sanofi, 598 U.S. 594 (2023) (No. 21-757) (failing to note the extent of Amgen's testing and stating that only twenty-six of the eighty-five antibodies found by Amgen were disclosed).

97 Arguably, depending on the wording of the patent, these may not be included in the claim, in which case complete disclosure is strictly true.

98 *See In re* Wands, 858 F.2d 731, 737 (Fed. Cir. 1988) (quoting *Ex parte* Jackson, No. 463-26, 217 U.S.P.Q. 804, 807 (B.P.A.I. Nov. 12, 1982)).

should belong in the database, this would not be sufficient to block enablement, as an inventor is "not required to predict all future developments which enable the practice of his invention."[99]

Where would this leave the Supreme Court's decision? On one hand, this case has every hallmark for which *Amgen v. Sanofi* was determined to require undue experimentation. On the other hand, this case requires substantively less experimentation than *Amgen*. In the end, *Amgen* does not provide enough broadly-applicable discussion to predict how this archetypical computational experimentation case would go.

B. The *Wands* Factors for Undue Experimentation

The Federal Circuit, in contrast to the Supreme Court, has given a set of concrete (though non-exhaustive) factors that allow patentees to know what qualifies as undue experimentation: the *Wands* factors. These eight factors have been regarded as "the key factors used to analyze enablement."[100] Though the Supreme Court has expressly condoned or controverted the use of the *Wands* factors, their language in *Amgen* has been noted to reflect some of them.[101]

Application of the *Wands* factors to computational experimentation leaves one obvious conclusion: computational experimentation is by its nature more enabling than traditional benchtop experimentation.[102] There is, however, substantial play in how such a conclusion is reached.

The first of the *Wands* factors regards the quantity of experimentation.[103] In a naïve sense, the strict number of experiments in computational experimentation is greater than traditional, as every successful candidate must go through both a computational and benchtop experiment. However,

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99 Hughes Aircraft Co. v. United States, 717 F.2d 1351, 1362 (Fed. Cir. 1983).

100 Shahrokh Falati, *Eviscerating Patent Scope*, 21 UIC REV. INTELL. PROP. L. 121, 165 (2022). Regardless of their prominence, other authors have called the *Wands* factors "misplaced and inapplicable in modern research where computational capabilities are pervasive." *E.g.* Tabrez Y. Ebrahim, *Computational Experimentation*, 21 VAND. J. ENT. & TECH. L. 591, 622 (2019).

101 3 DONALD S. CHISUM, CHISUM ON PATENTS § 7.03[4] (2023) (noting the similarity of the Court's word choice to factors 4 and 5).

102 Where necessary, the hypothetical from Part III.A, *supra*, will be invoked. However, much of what will be discussed here may be spoken of in general terms.

103 *In re* Wands, 858 F.2d at 737.

the quantity of time needed is weighed in this assessment,[104] as is the routine nature of this experimentation.[105] This tilts the balance wildly in the favor of computational experimentation. As described above,[106] the vast majority of candidates are done away with in the swift computational step, leaving only a few likely candidates to undergo the more time-consuming traditional step. Moreover, the computational step is extremely routine, often to the point of being totally automatable after the first run.

The second *Wands* factor, the amount of direction or guidance presented,[107] will vary substantially by field and patent. That said, computational experimentation generally has an edge here as well. Computational experimentation is governed by software, which is often well-documented. It is also bounded by the software, which has limitations on what it can utilize and output. Furthermore, computational experimentation typically features fewer steps of human intervention, and thus a lower need for guidance.

The third, fourth, and eighth *Wands* factors—the presence or absence of working examples, the nature of the invention, and the breadth of the claims, respectively[108]—all regard the patent application or the invention itself. They are not concerned with the process used to reach said invention and, thus, do not favor nor disfavor computational experimentation.

The fifth factor, the state of the prior art,[109] is difficult to assess without more case law regarding the application of this factor to machine learning.[110] It would also depend on what the court would determine the prior art to encompass. If the court determines that the prior art is the art in the field of the

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104 *See* Storer v. Clark, 860 F.3d 1340, 1351 (Fed. Cir. 2017) (invoking the "two year[]" time to synthesize a molecule in determine that the first *Wands* factor weighted against applicant).

105 *See* Idenix Pharms. LLC v. Gilead Scis. Inc., 941 F.3d 1149, 1156 (Fed. Cir. 2019) (listing "how routine any necessary experimentation is in the relevant field" as a consideration for the *Wands* factors).

106 *See* Part III.A, *supra*.

107 *In re* Wands, 858 F.2d at 737.

108 *Id.*

109 *Id.*

110 At date of writing, *In re* Starrett, No. 2022-2209, 2023 U.S. App. LEXIS 14231 (Fed. Cir. June 8, 2023) and Dialect, LLC v. Amazon.Com, Inc., No. 1:23cv581, 2024 U.S. Dist. LEXIS 156860 (E.D. Va. Aug. 30, 2024), are the only cases found when searching LEXIS or Westlaw for "Wands factors" and "machine learning." These cases are unreported, and neither substantively discusses the fifth *Wands* factor.

invention, then the use of computational experimentation is irrelevant. However, should the court instead rule that prior art concerns both the invention and the experimentation by which it is obtained, then the issue becomes far less predictable. For computational experimentation is a young art, much less mature than traditional experiments, thus disfavoring it in the light of the fifth factor. However, much of computational experimentation utilizes machine learning,[111] which arguably incorporates its entire training dataset as prior art, vastly favoring computational experimentation.

In terms of both case law and policy, the fifth factor is designed to allow the prior art to teach about how to use the patent specification—in other words, to fill in the holes left in the patent.[112] In this sense, the fifth factor disfavors computational experimentation, as its youth provides less art to teach users.[113] However, it should be noted that some more recent formulations of the *Wands* factors remove the fifth factor entirely in favor of a more general "nature and predictability of the field."[114]

The sixth factor, the relative skill of those in the art,[115] seems to fall inverse to the fifth. For if only the field of the invention is considered, then the sixth factor is even between computational and traditional experimentation. However, if instead the field of the experiment is analyzed, then the POSITA is clearly more skilled, as they must be skilled both on the benchtop and on the computer. Take Hantz and Lindert as an example. They had both the skill to test candidates on the benchtop, as a POSITA in the traditional experiment would, but also the skill to test candidates on the computational platform.

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111 *See, e.g.*, *AlphaFold*, *supra* note 71; Turzo, Hantz, & Lindert, *supra* note 16, at 1–12.

112 *See* Storer v. Clark, 860 F.3d 1340, 1346 (Fed. Cir. 2017); Martek Biosciences Corp. v. Nutrinova, Inc., 520 F. Supp. 2d 537, 557 (D. Del. 2007).

113 In the upcoming age of artificial intelligence, one may argue for the inclusion of the entirety of the machine learning dataset to be included in the prior art. This dataset, after all, is what allows the machine to form its predictions with such accuracy. This argument, however, borders dangerously close to arguing that the machine is an inventor, or at minimum a POSITA, an argument that has been disfavored by the courts. Thaler v. Vidal, 43 F.4th 1207, 1210 (Fed. Cir. 2022), *cert. denied*, 143 S. Ct. 1783 (2023).

114 Idenix Pharms. LLC v. Gilead Scis. Inc., 941 F.3d 1149, 1156 (Fed. Cir. 2019).

115 *In re* Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

Clearly, this level of skill must be greater than the level of skill for a traditional experimentalist.[116]

Finally, the seventh *Wands* factor is the predictability or unpredictability of the art.[117] Computational experimentation is noted as especially suited for the unpredictable arts.[118] Perhaps this is because computational experimentation substantially speeds up the results of unpredictable arts. Or, perhaps, it is because computational experimentation is a predictable field.[119]

This factor boils down to whether machine learning and software in general is predictable, and whether it can transform an unpredictable art into a predictable one. At least one author argues that the latter is the case. Ebrahim draws upon examples such as application of Monte Carlo simulations to metal organic frameworks and computationally created chemical intermediates.[120] In doing so, Ebrahim demonstrates that computational experimentation allows scientists to predict otherwise unpredictable results, such as nanocrystal pore size, chemical composition, and absorption properties, or properties of organic molecules based on the presence of functional key groups.[121]

Courts, by and large, seem to align software as a predictable art.[122] In their view, the arts lie on a scale from predictable to unpredictable, with mechanical and electrical engineering on the side of predictability, while chemistry is unpredictable.[123] Courts tend to analogize software with "the discipline of creating circuits in electrical engineering," making it predictable.[124]

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116 One may again forward the computer as one skilled in the art, much like with the fifth factor. However, this is likely to fail for the reasons given in note113, *supra*.

117 *In re* Wands, 858 F.2d at 737. This factor has been noted to be particularly important among the *Wands* factors. Greg R. Vetter, *Patent Law's Unpredictability Doctrine and the Software Arts*, 76 MO. L. REV. 763, 766 (2011).

118 *See* Ebrahim, *supra* note 100, at 606.

119 *But see* Vetter, *supra* note 117, at 787, 803–05 (stating "software technology is a predictable field like most areas of mechanical and electrical engineering," but later disputing this claim).

120 *See* Ebrahim, *supra* note 100, at 617–22, 625–27.

121 *Id.* at 618, 626. Ebrahim later argues that, in light of computational experimentation, the enablement requirement should be strengthened. *Id.* at 627.

122 *See* Vetter, *supra* note 117, at 787, 803.

123 *See* Karshtedt, Lemley, & Seymore, *supra* note 9, at 9–10.

124 Vetter, *supra* note 117, at 787, 803. Ultimately, all software truly is simply the result of machine code, which in turn is the result of preset circuitry. *See generally* RANDAL E. BRYANT & DAVID R. O'HALLARON, COMPUTER SYSTEMS (2d ed. 2011). Thus, within minimal chance of spontaneous error, the termination is a set result

Here, experts disagree quite loudly. Humelsine argues that "software [is] still as much an art as science" and that "as a [programming] project's size and complexity grow, its behaviors become less rigorous."[125] Larus and Hunt contradict the prevailing attitude of the courts that software is similar to electrical engineering by indicating that Microsoft views modern software as separate from engineering.[126] Especially in the field of artificial intelligence, experts like Kentaro Toyama argue that software is unpredictable and may forever remain so.[127]

Where does all this leave computational experimentation? Two of the *Wands* factors tip considerably in its favor, two factors are in strong contention with each other, and one factor has courts disagreeing with experts. In total, the *Wands* factors report that computational experimentation is notably more enabling than traditional benchtop experimentation.

But is this strong enough to merit a genus claim, on a class of drugs, for example? A genus claim clearly shifts factors (1) and (8) toward undue experimentation, but to what result? This is clearly fact-specific, so let us return to the hypothetical of Hantz and Lindert and the comparison to *Amgen*.

In *Amgen*, the district court found that the patent required substantial experimentation (factor (1));[128] that there was direction and working examples provided, but they gave no "significant guidance" (factors (2) and (3));[129] that the nature of the invention, the prior art, and the skill of a POSITA were all such that they were enabling of the claim (factors (4)–(6));[130] that the

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like in electrical engineering. However, this simplification is fallacious. It would be equally true to say that chemistry is merely the result of applied physical principles, and thus has a set, knowable result. The fallacy in both of these reductive actions is in the knowability of the complete starting conditions and the complex ways that they may interact.

125 Jim Humelsine, Letter to the Editor, *Software Still as Much an Art as Science*, 53 COMMUN. ACM 7, 7 (2010), https://doi.org/10.1145/1629175.1629178 [https://perma.cc/4G65-WLDA].

126 *See* James Larus & Galen Hunt, *The Singularity System*, 53 COMMUN. ACM, 72, 72 (2010), https://doi.org/10.1145/1787234.1787253 [https://perma.cc/WXH9-QQYT] ("The Singularity Project at Microsoft Research began by asking what modern operating-system and application software would look like if it were designed with modern software-engineering practices and tools.").

127 Andréa Morris, *AI Concepts Are Alien Shapes*, FORBES (July 5, 2023, 2:00 PM), https://www.forbes.com/sites/andreamorris/2023/07/05/the-paradox-of-predicting-ai-unpredictability-is-a-measure-of-intelligence/ [https://perma.cc/6X6F-EWGF].

128 Amgen Inc. v. Sanofi, No. 14-1317-RGA, 2019 U.S. Dist. LEXIS 146305, at *32–35 (D. Del. Aug. 28, 2019).

129 *Id.* at *28–32.

130 *Id.* at *27–28.

art was unpredictable (factor (7));[131] and that the claims were vast (factor (8)).[132] For Hantz and Lindert, factors (4)–(6) would be much the same, if not slightly more enabling, and factor (8) would be equally vast. The remaining factors, though, tend to differ.

Amgen left the remainder of the world of antibodies to others as a "research assignment[]."[133] The same cannot be said for Hantz and Lindert. They have already checked an entire database of drug-like small molecules, and derivatives of that database. Other than synthesis of the reported viable drugs, it may be argued that there is no experimentation left to be done. Where such experimentation remains, the computational portion would make the process far more swift and routine than in *Amgen*. Certainly, this requires nowhere near the "substantial amount of time and effort" that Amgen did.[134]

Hantz and Lindert also provide more guidance than Amgen, though perhaps not enough to reach "significant guidance." As discussed above, computational experimentation inherently provides more guidance than benchtop experimentation, through the benefit and restrictions of software. Furthermore, Hantz and Lindert presumptively provided the entirety of working species in their claim, while Amgen self-admittedly did not.[135] If the court is willing to accept that Hantz and Lindert disclosed all working species in their claim, then this disclosure certainly forms "significant guidance." If not, then Hantz and Lindert face similar complaints to Amgen, for they provide minimal guidance to "teach a person of ordinary skill in the art how to predict" a working species and give instructions significantly similar to Amgen's "roadmap."[136]

In *Amgen*, the district court indicated that the correct test for predictability is whether, when looking at a candidate species, a person would know whether or not it met a functional limitation.[137] The court even goes as far as to imply that one should not consider the maturity of the art or the skill of those

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131 *Id.* at *23–27.

132 *Id.* at *19–23.

133 Amgen Inc. v. Sanofi, 598 U.S. 594, 614 (2023).

134 *Amgen*, 2019 U.S. Dist. LEXIS 146305, at *35.

135 *See* Petition for Writ of Certiorari, *supra* note 96, at 8 (stating that only twenty-six of the eighty-five antibodies found by Amgen were disclosed).

136 *Amgen*, 2019 U.S. Dist. LEXIS 146305, at *28–29, *31.

137 *See id.* at *23–24.

in the art.[138] While cutting well to the heart of the matter, this seems to be either an oversimplification or in dissent with other courts. Mechanical engineering has been established to be a predictable art, and yet a mechanical engineer cannot look at a wooden bridge and say if it can support a car without substantial details and computation.[139] But there does seem to be some core truth that the court is reaching out to. For, relevant to the case, it is not understood how to make an antibody have the correct shape for an intended function, and thus such a relationship is unpredictable.[140]

This is equally true for Hantz and Lindert. Indeed, it is equally true for all medication which doesn't have a well-known function.[141] In this sense, the court seems to argue that it truly is the predictability of the art of the invention itself, not the art of the experimentation, thus implying that the use of computational experimentation is irrelevant. If another court were to disagree, would that help Hantz and Lindert? Above it was argued that it might. However, that court might agree with experts on the unpredictability of software, and rule that simply adding an unpredictable layer on top of an unpredictability does not make an art more predictable.

After all this, where are Hantz and Lindert left standing? Again, certainly better off than Amgen. They require substantially less experimentation and are more enabling with their guidance and provided disclosures.

Is it enough? I argue yes. It is hard to imagine what more Hantz and Lindert, or another pair in substantially the same shoes, could do to enable. They've swept the entirety of a significant database of drug-like small molecules. They've disclosed their entire process, a process that a POSITA would be able to follow. And they've specified all confirmed candidates within their disclosure. Even in a highly analogous case like *Amgen*, the Court refused to say that no such genus claims

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138 *See id.* at *24. This would imply that, for predictability standards, we are indeed looking at the abilities of a regular person to predict, as a POSITA would presumptively have knowledge of the prior art and would definitively be a person of ordinary skill in the art.

139 A regular person would be even more hopeless at such a task than this beleaguered mechanical engineer.

140 *Id.* at *27.

141 Of course, medication with a well-known function would be impossible to patent under the novelty bar.

could be made.[142] If they still anticipate such a claim to be available, what better claim than this?

Of course, perhaps even this is not enough. Perhaps more candidates need to be searched, unlikely as they may be. Perhaps the time is simply not yet right, and the state of the art and the skills of those therein need to mature. Or perhaps such a claim is simply not possible. Perhaps the court would require a "rule of thumb" to detect viable candidates, which may not exist in reality. Perhaps, due to the functionally infinite number of drug candidates, no sufficient search could be run. In other words, perhaps within the requirement for enablement is a silent bar on patentable subject matter, a bar that prevents genus claims of drugs, and an entire genus of other genus claims with it.

IV
SALVAGING NON-OBVIOUSNESS

Thus far, the discussion has been limited to the enablement of genus claims. However, enablement and obviousness have a difficult relationship for the patentee. Recall the factual inquiries for obviousness as established in *Graham*: (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; and (3) the level of ordinary skill in the pertinent art. These are exceptionally similar to the fifth and sixth *Wands* factors. Furthermore, the MPEP repeatedly stresses the predictability in the art, as does the seventh *Wands* factor.[143] Put more generally, arguments for increased enablement may also risk the patent by arguing for obviousness.[144]

Computational experimentation certainly poses a risk here. The general argument would go as follows. (1) All feasible starting conditions are published and analogous, (2) the computational methods are published and analogous, and (3) the desired final result is known. As a result of these three premises, a POSITA can apply the computational method until they find a starting condition that results in the desired final result. Drug discovery methods are especially subject to this pathway,

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142 *See* Amgen Inc. v. Sanofi, 598 U.S. 594, 613 (2023).

143 *See* MPEP, *supra* note 38, § 2141.III (repeatedly stating predictability in the listed rationales for a finding of obviousness).

144 *See generally* Matt Lincicum, *A Knot in the Eternal Golden Braid: Searching for Coherence in the Relationship Between Enablement, Anticipation, and Obviousness*, 23 HARV. J.L. & TECH. 589, 598–600 (2010).

as the successful starting condition (a drug candidate) is one of the most desired patents, and therefore the only issue barring patentability is the knowing which drug(s) will result in the desired behavior.

This would likely be insufficient to block a claim for any individual drug or set of specified drugs.[145] Although the knowledge may exist in some sense—a POSITA could always apply computational experimentation to the given drug—it is difficult to argue that there is prior art describing that any particular drug or set of drugs would be effective simply because a method could discover them.[146] An inventor needs to take the final "inventive step."[147]

However, a genus claim, as structured above, does not have the same protection. The inventive step is not finding the particular drug that is effective, but simply using computational experimentation methods to find all, if any, drugs that work. This is much closer to a claim of obviousness, as a POSITA would know of the drug candidates and would know how to apply the computational method to these drug candidates. As such, though genus claims may no longer die to enablement, they may fall to obviousness.

Can the genus claim be salvaged? Reading into the *Graham* factors, things seem pessimistic. Inventors would be drawing from published prior art and published methods, both of which are likely to be used in a way very similar to prior publications. This weighs the first two factors against genus claims. The third factor is equally bad, as a POSITA would certainly know how to apply the computational method to the class of metabolites.

There are some slight alterations that could be made to avoid this problem. The inventor could use a new and nonobvious set of starting conditions, ideally one that is larger or

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145 *But see* Matthew Chun, *Artificial Intelligence for Drug Discovery: A New Frontier for Patent Law*, 104 J. PAT. & TRADEMARK OFF. SOC'Y 5, 32–33 (2024) (acknowledging and dismissing arguments that artificial intelligence will make all drug discovery obvious).

146 Patentability as a whole requires this premise. Nearly all inventions are derived from prior knowledge at some point. Forbidding patents because the knowledge exists for someone to combine and exploit would thus fully uproot a patent system.

147 Other nations and international treaties use the term "inventive step" in place of "non-obviousness." *See* Lee Petherbridge, *Intelligent TRIPS Implementation: A Strategy for Countries on the Cusp of Development*, 22 U. PA. J. INT'L ECON. L. 1029, 1043–44 (2001). Here, the terms are used interchangeably, as the phrase "inventive step" may be more instructive to the reader.

better targeted.[148] The inventor could use a new computational method. Or the inventor could target a final result in a way not known to the public, such as targeting a novel protein for drug discovery. Each of these would remove a form of prior art necessary for a finding of obviousness from consideration, and thus render the claim non-obvious (at least on these grounds).

The claim may still be sustainable even if it doesn't use something completely novel. As in the Hantz and Lindert hypothetical above, the patentee could run the full experiment themselves to confirm as many successful candidates as possible. This should be the whole genus, or nearly all of it. As such, the inventive step would have already been taken, analogously to the argument for single drug claims above.[149]

Courts have also given tacit approval to non-obviousness in genus claims. The District Court for the District of Delaware granted JMOL to Amgen with regard to non-obviousness in the same case that would eventually be found as non-enabling by the Supreme Court.[150] This decision was appealed on a technicality dealing with provisional patent applications.[151] However, this appeal was denied, and moreover the obviousness of the "roadmap" was not taken to the Federal Circuit.[152]

Nonetheless, this is untrod ground. While patentees may take some umbrage in Amgen's genus claim not being invalidated due to their commonly-understood "roadmap," arguing that computational experimentation is more enabling will also weaken the argument it is non-obvious. As a result, genus claims taking this route will require a well-crafted patent in order to survive challenges of this stripe.

CONCLUSION

In the discussion of Hantz and Lindert's hypothetical patent, a few important details have been glossed over. The most obvious may be the option for them to only patent the twelve

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148 Non-obviousness is especially important in this path, as there are many simple and obvious ways to combine pre-existing sets of starting conditions or otherwise deriving new starting conditions from ones in a pre-existing set (such as generating different stereoisomers in drug discovery).

149 Importantly, the patentee would not want to argue that the result of the experiment is unpredictable, as this directly damages their undue experimentation argument.

150 Amgen Inc. v. Sanofi, No. 14-1317-RGA, 2019 U.S. Dist. LEXIS 146305, at *2–3 (D. Del. Aug. 28, 2019).

151 Amgen Inc. v. Sanofi, 872 F.3d 1367, 1380 (Fed. Cir. 2017).

152 *See id.*

drugs they discovered—which they believed to be the only drugs that inhibited CSF1R. This option was ignored, in no small part, because it ignored the point of the hypothetical, but also because only attempting to claim these few drugs would be poor patent practice. Patents, after all, also protect their holders from future developments,[153] and it would be in the holder's interest to extend the patent protection as much as possible. Further, it is entirely plausible for Hantz and Lindert to claim both the genus and the specific species of drugs in different claims.

Additionally, the other requirements for a patent were simply granted to be satisfied. Such ease is far less likely outside the world of hypotheticals. If poorly crafted, a genus claim may run into issues with having a specific, known benefit for utility, and may be anticipated or obvious. Indeed, the Court in 1895 noted that Sawyer and Man's genus claim in *Incandescent Lamp Patent* would have defeated itself on anticipation grounds even had it survived undue experimentation.[154]

But perhaps a better question is whether such genus claims should be allowed. Most authors agree that they should. Karshtedt, Lemley, and Seymore argue that genus claims are important and well suited to the chemical industry, and thus should be permitted.[155] They further assert that these genus claims are only used by those industries in order to prevent competitors from taking a part of an innovator's patent and making a minor change to avoid infringement.[156] Franzosa puts forward that life science companies rely on genus patents to "ensure the profitability of their research and development efforts, encourage investors to maintain funding, and bring effective products to the market."[157] Falati argues for a novel approach to § 112(a) in order to save genus claims and make the law "technologically neutral."[158] Lukacher asserts that we should return to the PTO's guidelines and allow genus claims whenever a POSITA would understand the scope of the claimed invention.[159]

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153 Hughes Aircraft Co. v. United States, 717 F.2d 1351, 1362 (Fed. Cir. 1983).

154 The Incandescent Lamp Patent, 159 U.S. 465, 476–77 (1895).

155 Karshtedt, Lemley, & Seymore, *supra* note 9, at 3–5.

156 *Id.* at 3.

157 Alexander Franzosa, *The Supreme Court's Missed Opportunity to Save Genus Claims in Life Science Patents*, 2023 B.C. INTELL. PROP. & TECH. F. 1, 2 (2023).

158 *See* Falati, *supra* note 51, at 289–93.

159 Anna N. Lukacher, *The Future of Patenting Antibodies after* Amgen v. Sanofi, 58 IDEA 95, 129 (2017).

Not all authors agree. Lemley and Sherkow argue for a middle ground so as to avoid broad patent protection from inhibiting innovation.[160] Jakas asserts that genus claims should be restricted so that the patent only protects what an inventor actually discovered instead of "receiving broad genus patents that may cover discoveries that they have not yet made."[161]

Regardless of the changes in patent law, a certainty is that computers will continue their encroachment in every aspect of life. It was not that long ago that calculators were not commonplace. Programmable computers are less than a century old.[162] Fully CGI movies are less than three decades old.[163] All of these revolutions meant substantial change for science, offloading grunt work previously done by hand and significantly changing the nature of how experiments are done. It should not be surprising that computational work will continue to offset experiments until only the minimal benchtop work is done.

As we approach that day, the standards for patents will swiftly change, even if patent law statutes remain stationary. They have already changed substantially—we are seemingly eras away from sending a messenger to far-off Asia in order to gather bamboo samples. We may already be in a world where, given modern commerce and communication, Sawyer and Man's claim would have survived undue experimentation with sparse more disclosure. As a result of such enablement, perhaps we are at a point where genus drug claims can survive to be enforced against infringers.

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160 Mark A Lemley & Jacob S. Sherkow, *The Antibody Patent Paradox*, 132 YALE L.J. 994, 1000 (2023).

161 Joseph Jakas, *Encouraging Further Innovation:* Ariad v. Eli Lilly *and the Written Description Requirement*, 42 SETON HALL L. REV. 1287, 1334 (2012).

162 *See* Erica K. Brockmeier, *The World's First General Purpose Computer Turns 75*, PENN TODAY (Feb. 11, 2021), https://penntoday.upenn.edu/news/worlds-first-general-purpose-computer-turns-75 [https://perma.cc/7EYF-2FL6].

163 *See* Julia Zorthian, *How Toy Story Changed Movie History*, TIME (Nov. 19, 2015 1:30 PM), https://time.com/4118006/20-years-toy-story-pixar/ [https://perma.cc/NFP5-9XW3].