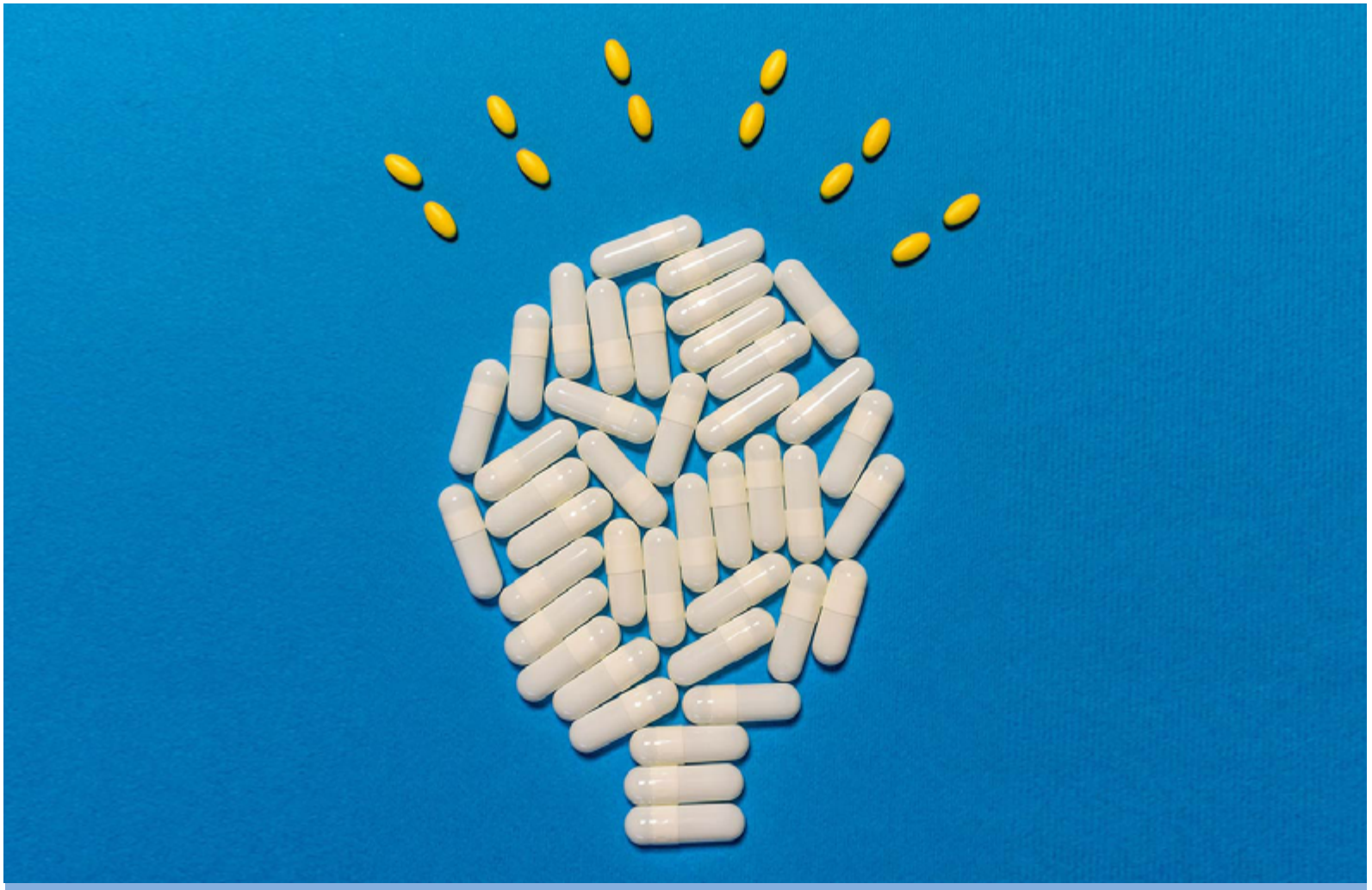

PATENT LAW CONSIDERATIONS FOR DRUG DISCOVERY INNOVATIONS UTILIZING ARTIFICIAL INTELLIGENCE

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By Carl Kukkonen, Patricia Campbell & Gurneet Singh

Taking a drug to market is a complex process that involves prediction of one or more combinations of molecules that can be transformed into a drug, and performance of experiments on each molecular combination to test for efficacy, stability, safety, and other metrics. This road of trial-and-error experimenting with different molecular combinations can take many years, and cost billions of dollars. Artificial intelligence ("AI") tools can substantially reduce the time of trial-and-error experimenting with molecules by trimming the molecules that are not ideal based on historical data. This quickens the process and reduces the investment for finding effective, stable, and safe molecular combinations that can be developed into a drug. This article elaborates on the confluence of drug discovery and AI, some industry partnerships between pharmaceutical and AI companies, implications of pharma-AI confluence for patent law, and various recommendations for protecting technological aspects of the pharma-AI confluence.

01

DRUG DISCOVERY AND ARTIFICIAL INTELLIGENCE

In the pharmaceutical and biopharmaceutical industries, taking a drug to market is a tedious process. For example, to create a drug, scientists first predict one or more combinations of molecules that can be transformed into a drug. Next, scientists perform experiments on each molecular combination to test for efficacy, stability, safety, and other metrics. Many promising molecular combinations fail one or more metrics. This road of trial-and-error experimenting with different molecular combinations can take many years, and cost billions of dollars.

Artificial intelligence ("AI") tools have been proven to substantially reduce the time of trial-and-error experimenting with molecules by trimming the molecules that are not ideal based on historical data. Particularly, AI tools can sift quickly through stores of data and results from decades of laboratory experiments to suggest molecular combinations with the desired characteristics that are optimized for a specific medicinal task. Pharmaceutical companies can fast-track those suggested molecular combinations, also referred to as leads, for determining efficacy, stability, safety, and other metrics. This quickens the process and reduces the investment for finding effective, stable, and safe molecular combinations that can be developed into a drug. AI can help new drugs reach the clinical stage five times faster and cut industry costs by 30 percent.[2]

In addition, AI allows for expeditiously repurposing drugs (also referred to as drug repositioning, reprofiling, or retasking).[3] Drug repurposing is a strategy for identifying new uses for approved or investigational drugs that are outside the scope of the original medical indication.[4] Repurposing qualifies an existing drug directly for Phase II clinical trials, thereby reducing the time and investment otherwise required for drug development. For example, repurposing significantly diminishes expenditures because, for example, the cost of launching a new drug typically amounts to $41.3 million, while relaunching an existing drug typically amounts to only $8.4 million.[5]

For drug discovery and development,[6] AI has accelerated drug screening (including target identification and validation), design (through access to new biology or improved / novel chemistry), validation, and repurposing, among other uses. Drug screening includes prediction of bioactivity and toxicity. Bioactivity, as in the level of binding between a material and living tissue, is a critical factor in determining the effectiveness of a drug molecule. In order to deliver a therapeutic response, drugs must have adequate affinity for target proteins or receptors. Alternatively, a drug that interacts with unintended proteins or receptors can lead to toxicity. AI can measure the binding affinity of a drug based on features measuring similarity between the drug and a target, intended or unintended.[7]

For designing drug molecules, AI can be used to predict the three-dimensional protein structure and ensure the resulting drug is designed in accordance with the chemical environment of a target protein site.[8]

For clinical trial design and monitoring,[9] AI has been used to enroll or select subjects, and to facilitate patient compliance or dropout. Improper patient selection and patient dropout respectively contribute to 86 percent and 30 percent of clinical trial failures.[10] Given the substantial time (about 6 to 7 years) and financial investment dedicated to clinical trials, a clearance rate of only about 10 percent of drug candidates in trial represents a monumental loss to the pharmaceutical industry.[11] AI can improve the success rate by limiting the recruitment of the disease population to patients with the necessary drug targets. For patient dropout, AI has been used to monitor

2 http://www.pmlive.com/pharma_intelligence/Has_AI_been_the_key_to_tackling_the_COVID-19_pandemic_1346052.

3 *Id*.

4 https://www.nature.com/articles/nrd.2018.168#:~:text=Drug%20repurposing%20(also%20called%20drug,drug%20for%20a%20given%20indication.

5 https://www.pmlive.com/pharma_intelligence/Has_AI_been_the_key_to_tackling_the_COVID-19_pandemic_1346052.

6 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7577280/.

7 *Id*.

8 *Id*.

9 *Id*.

10 *Id*.

11 *Id*.

medication intake of schizophrenia patients in a Phase II trial, which increased the adherence rate of patients by 25 percent and ultimately led to the successful completion of the trial.

AI has also been employed in manufacturing by correlating manufacturing errors to set parameters and by performing various automation functions; in product management by evaluating market positioning criteria, performing market prediction and analysis, and determining product costs; and in quality assurance and quality control through understanding critical process parameters, guiding future production cycles, and regulating in-line quality.

02
PHARMACEUTICAL AND AI PARTNERSHIPS

Over the last five years, interest in and use of AI in several sectors of the pharmaceutical and biopharmaceutical industry has rapidly increased and continues to grow. By the end of 2022, AI-facilitated solutions in the pharmaceutical sector are projected to achieve a revenue of over $2 billion.[12]

The burgeoning interest in AI's applications in pharmaceuticals makes sense as AI can help new drugs reach the clinical stage five times faster and cut industry costs by 30 percent.[13] For example, AI can predict drug-target interactions, which allows for the repurposing of existing drugs.[14] Repurposing qualifies an existing drug directly for Phase II clinical trials. This qualification eliminates the time investment otherwise required for three major stages of drug development namely, drug discovery, the preclinical phase, and Phase I clinical trials. Further, repurposing significantly diminishes expenditures because the cost of launching a new drug typically amounts to $41.3 million, while relaunching an existing drug typically amounts to only $8.4 million.[15]

Traditionally, pharmaceutical companies and AI platform companies have been separate. To enhance speed and reduce cost during drug discovery and development, pharmaceutical-AI partnerships between several industry leaders in the pharmaceutical and AI spaces continue to emerge.

In late 2019, Novartis selected Microsoft as its AI partner in its research on cell and gene-based therapies with the collaboration seeking to speed the process of developing medicines from years to potentially weeks or even days.[16]

At the start of 2022, Sanofi agreed to pay $100 million upfront with a potential $5.2 billion in downstream milestones for rights to up to 15 oncology and immunology drugs to be identified by Exscientia's AI technology.[17] Sanofi also recently, in August 2022, invested in AI-powered drug discovery by inking a $1.2 billion biobucks research collaboration with San Francisco-based Atomwise.[18]

AstraZeneca, GlaxoSmithKline, Biogen, Bayer, and Novartis have similarly entered into deals with Ionis Pharmaceuticals, which has developed a drug discovery platform that targets RNA to create new antisense therapies.[19]

Biopharmaceutical and artificial intelligence partnerships have considerable potential for success and are expected to generate revenues of over $44.5 billion by 2026.[20]

12 https://www.researchandmarkets.com/reports/4846380/growth-insight-role-of-ai-in-the-pharmaceutical.

13 https://www.pmlive.com/pharma_intelligence/Has_AI_been_the_key_to_tackling_the_COVID-19_pandemic_1346052.

14 *Id*.

15 *Id*.

16 https://news.microsoft.com/transform/novartis-empowers-scientists-ai-speed-discovery-development-breakthrough-medicines/.

17 https://endpts.com/sanofi-exscientia-ink-the-next-ai-megadeal-signing-terms-on-a-100m-upfront-pact-with-up-to-15-drugs-on-the-line/.

18 https://www.fiercebiotech.com/biotech/sanofi-signs-12b-pact-atomwise-latest-high-value-ai-drug-discovery-deal.

19 https://www.fiercebiotech.com/special-report/top-10-m-a-targets-biotech-for-2022.

20 https://www.prnewswire.com/news-releases/healthcare-artificial-intelligence-ai-market-size-to-reach-revenues-of-usd-44-5-billion-by-2026--arizton-301435270.html.

03
IMPLICATIONS FOR PATENT LAW

The confluence of AI and pharmaceuticals involve new inventions that can be protected using patent law, implications of which are discussed below.

A. Nonobviousness

One requirement for U.S. patent protection is for the invention to be nonobvious. 35 U.S.C. § 103. Whether an invention is obvious is analyzed through the eyes of a hypothetical person of ordinary skill in the art ("POSITA"). Essentially, if the differences between the invention seeking a patent and the prior art (any materials publicly disclosed prior to the patent's filing date) would have been obvious to a POSITA, the USPTO will not award a patent to the applicant. For example, using a new material like porcelain for a wooden doorknob would be "obvious" to a POSITA. *Hotchkiss v. Greenwood*, 52 U.S. 248 (1850). There must be proof of "more ingenuity and skill . . . than were possessed by an ordinary mechanic acquainted with the business."

In the context of AI-facilitated biopharmaceutical solutions, determining who is the POSITA is not always clear. AI systems require large interdisciplinary teams for programming, training, and perfecting code. Is the POSITA the AI programmer or the technician in the field of the invention? One issue, however, is settled. The Supreme Court has affirmed that the POSITA is not an automaton,[21] so there can be no "AI of ordinary skill in the art."[22]

There are also concerns over whether AI recalibrates the obviousness standard since AI increases what a POSITA has the capacity to recognize as obvious.[23] The American Intellectual Property Law Association posited that what seems nonobvious to a human "could be rather obvious to an artificial intelligence machine because it has the capability to crunch through a bunch of numbers in a very fast period of time and come up with an answer to a problem in minutes that would take a human being a lifetime." The SUNY Research Foundation considered accessibility issues and suspected that accounting for AI's capacity would make it "impossible for everyday inventors without access to artificial intelligence to make a patentable contribution to their respective, far-ranging fields."

B. Inventorship

Under U.S. patent law, inventorship determines patent ownership. There is widespread debate over whether artificial intelligence can be considered an inventor for purposes of securing a patent. A key area of the debate focuses on whether AI is simply a tool or something more. One of the essential criteria for inventorship is conception that goes beyond supplying abstract ideas or merely executing others' ideas.[24] Conception is about abstract thinking, an ability that even the world's most sophisticated forms of AI currently lack.

Computer scientist Stephen Thaler is the human inventor of DABUS, an AI machine that "invented" an improved beverage container and a device for search-and-rescue missions.[25] In 2019, Thaler filed patent applications listing DABUS as the sole inventor for these devices in over a dozen countries and the European Union. With these application, Thaler and his international legal team have argued around the world that AI should be considered an inventor for the purposes of receiving a patent with varying results.

On August 5, 2022, in *Thader v. Vidal*, the U.S. Court of Appeals for the Federal Circuit affirmed that patent inventors must be natural persons, rejecting a technologist's attempt to name an artificial intelligence as the sole inventor on patent applications. In this opinion, the Federal Circuit affirmed actions by lower courts and the U.S. Patent and Trademark Office, holding once again that patent inventors can only be natural persons. The Patent Act defines inventors as "the individual or . . . individuals collectively who invented." 35 U.S.C. § 100(f). As a result, whether "individual" could include non-persons such as an AI was a matter of statutory interpretation, and the analysis was a simple one. Because the Supreme Court has held that an "individual" generally means a human being absent some indication that Congress intended a different meaning, and because the Patent Act offers no such indication, the Federal Circuit held that the statute is unambiguous in restricting inventors to natural persons. Thus, according to the Court, no complicated inquiry into the nature of invention, or the rights of AI, was required.

21 https://www.westlaw.com/Document/Ie2b011acf72211dbb92c924f6a2d2928/View/FullText.html?transitionType=Default&contextData=(sc.Default)&VR=3.0&RS=cblt1.0.

22 https://revistajuridica.uprrp.edu/inrev/index.php/2021/10/28/its-time-for-the-ai-patent-the-case-for-an-artificial-intelligence-patent-category/#easy-footnote-bottom-52-3257.

23 https://news.bloomberglaw.com/ip-law/patents-and-artificial-intelligence-an-obvious-slippery-slope.

24 https://academic.oup.com/grurint/article/71/4/295/6528412.

25 *Id*.

In contrast to the U.S., a Federal Court of Australia judge agreed with Thaler,[26] finding that Australian patent provisions do not preclude AI systems from being treated as inventors and opining that failing to recognize AI inventorship would harm innovation. However, Australia's second highest judiciary body, the Federal Court of Australia's Court, realigned Australian patent law with the rest of the world and reversed the lower court's decision.[27] The court referenced language from Australia's highest court that repeatedly used "human action" to define patent eligible subject matter.

In the artificial intelligence and legal communities, the majority viewpoint is that AI techniques are merely tools in a human inventor's hands.[28] While the artificial intelligence community has expressed criticism of the anthropomorphization of AI, some have persuasively argued that AI is simply a tool when a human uses AI to facilitate the inventive process in the same way as one would use any other tool like a microscope.[29] There, the inventor would be the person using the AI, not the individual who developed the AI algorithm. In other words, patent law recognizes an inventor in the individual who engaged in thinking and decision-making to solve problems assisted by AI.[30] That individual would be the researcher or scientists screening, developing, and discovering drugs in the biopharmaceutical context. Not the one who developed the basic AI algorithm of a general-purpose nature. Additionally, if "mere implementation of instructions" would not suffice for a human inventor to be entitled to a patent, AI creating output from human input cannot be a standalone inventor either.

Even if inventorship were to be recognized in AI, the question of ownership would remain. In cases where the patent applicant is different from the inventor, the patent applicant must show it properly obtained ownership from the inventor. This was the case in Thaler's patent applications around the world, listing DABUS as the inventor. An AI machine like DABUS can neither hold title to an invention nor pass title to a patent applicant like Thaler under current U.S. patent law.

> ***Computer scientist Stephen Thaler is the human inventor of DABUS, an AI machine that "invented" an improved beverage container and a device for search-and-rescue missions***

Critics of the world's majority position of inventorship believe that this stance makes AI-facilitated inventions and discoveries unpatentable.[31] Some have suggested turning to trade secrets, which offers the advantages over patents of not requiring public disclosure and retaining protection for unlimited periods of time.[32] As long as an invention can be protected by employing reasonable measures to maintain it as a secret, the trade secret will offer protection. However, this is less appropriate in the pharmaceutical context, where securing FDA approval for a drug requires disclosure of its ingredients, what happened during the clinical trials, and its manufacturing, processing, and packaging, which makes trade secret protection unworkable.[33]

26 https://www.judgments.fedcourt.gov.au/judgments/Judgments/fca/single/2021/2021fca0879.

27 https://www.law360.com/ip/articles/1483893/australian-appeals-court-says-ai-actually-can-t-get-patents.

28 https://www.law360.com/ip/articles/1483893/australian-appeals-court-says-ai-actually-can-t-get-patents.

29 https://www.twobirds.com/en/insights/2019/global/who-owns-an-ai-generated-invention.

30 *Id*.

31 https://montrealethics.ai/summoning-a-new-artificial-intelligence-patent-model-in-the-age-of-pandemic/.

32 https://revistajuridica.uprrp.edu/inrev/index.php/2021/10/28/its-time-for-the-ai-patent-the-case-for-an-artificial-intelligence-patent-category/.

33 https://www.fda.gov/drugs/types-applications/new-drug-application-nda.

04

ADDITIONAL RECOMMENDATIONS FOR PROTECTING TECHNOLOGICAL ASPECTS OF AI-PHARMA PARTNERSHIPS

Companies should consider the following when strategizing on protecting their AI by way of patents.

First, innovators should have a framework to harvest AI inventions for patenting. For example, it can be helpful to classify and harvest the inventions based on the stage in the AI process. Such stages include, for example:

- building a machine learning ("ML") model (e.g. identifying types of input and output of the ML model and specifying functions to be performed by the ML model),
- obtaining training data for the ML model (which can include training inputs fed into the ML model to train the model, and categories for such training inputs such that the ML model is trained to identify a training input as belonging to a respective category),
- training of the ML model (which is generally an iterative process that determines model weights to optimize some objective function that identifies a training input as belonging to a respective category),
- hosting the trained ML model and providing access to the trained ML model (e.g. hosting the ML model in a cloud and providing remote access to it on a user device),
- deploying the trained ML model to generate a predicted output (e.g. executing the trained ML model on real or live input to predict an output such as a category to which the input belongs), or
- application of the predicted output (e.g. system that takes, as input the predicted output generated by the ML model to perform some further processing).

Second, companies should consider whether their AI innovations are eligible for patenting. The U.S. Supreme Court's decision in *Alice* and subsequent decisions by the Federal Circuit, as well as guidance published by the U.S. Patent and Trademark Office (USPTO), have provided guidance on subject matter eligibility (SME) that applies to AI inventions. Based on this guidance, life-sciences companies should, in general, steer away from merely disclosing mathematic relationships or formulas, mere ideas that can reside within the mind of the inventors, or just ideas of organizing human activity, and should rather, or additionally, focus on technological or computational improvements offered by implementation of their AI innovations.

Third, even if their AI is patent-eligible, innovators should consider whether they should patent the AI or maintain it as a trade secret. To make this determination, companies can consider factors including tenure of protection, public disclosure, investor value, damages, and SME. For tenure, patents have a limited life, which in the U.S. for utility patents is 20 years from the earliest filing date, whereas the trade secrets can be maintained for an indefinite time so long as the companies maintain secrecy. However, given the speed at which technology advances or modifies nowadays, the limits on the tenure do not deter patent protection. Public disclosure can be an important factor for sensitive cases because the patents disclosing AI inventions may become public at some point before the patent even issues. However, for patents being filed only in the U.S., patentees can delay the publication until issuance of the patent by filing a non-publication request. With respect to investor value, patents allow easier ways to analyze and quantify the value of the AI innovations, whereas it is generally more difficult to quantify the value of a trade secret. For damages, there can be high hurdles to prove and obtain patent damages, while monetary relief may be easier to obtain once trade secret misappropriation has been established. From the SME perspective, some AI aspects, such as training data used to train ML models, may not be patent-eligible by itself, and may be better protected by way of trade secrets.

Fourth, if companies pursue patent protection, it is important to consider when to file patents. There has generally been a "land rush" to file AI patents. Given this trend and the fact that most jurisdictions, including the U.S., have a first to file patent system, companies can benefit by filing sooner rather than later.

Fifth, innovators should decide on subject matter to be presented in the patent claims such that it's relatively easy to identify infringement. For example, a technique for training an ensemble of machine learning models for drug discovery purposes might be a candidate for treatment as a trade secret given the potential difficulty of identifying competitor infringement. In other cases, patent protection might be more appropriate if the innovation is consumer facing (e.g. a digital health platform, etc.), can be reverse engineered without much burden, competitors publish their activities, and there are few or no alternative approaches to practicing the invention.

05
CONCLUSION

Artificial intelligence has many valuable applications that can accelerate and reduce the cost of discovery in the biopharmaceutical industry. Upholding patent protections for new AI-facilitated inventions will advance threaten life-saving discoveries and innovation. So long as human ingenuity continues to lead biopharmaceutical development and discovery, with AI as a tool rather than as a replacement for human creativity, patent protection will remain viable and should be pursued strategically.

> *...tors should decide on subject matter to be presented in the patent claims such that it's relatively easy to identify infringement*

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