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# 7 Hot Topics in IP for Pharma AI and Bioinformatics

IP strategies for life sciences and big data have typically followed two very distinct paths. Some practitioners and stakeholders have recently started to call for changes to our current unitary patent system, possibly creating different patent systems and requirements for pharma/life sciences and software. But over the last decade, and especially the last five years, those two worlds have been converging via technological advances in bioinformatics, pharma AI, and personalized medicine. In no particular order, this article highlights seven key concerns facing practitioners in this cross-disciplinary space.

## 1. What's the value of an AI patent to the life sciences industry?

Setting aside questions regarding patentability and patent eligibility, all applicants in the pharmaceutical and diagnostics industries should ask whether a software-based patent presents the best return on investment for their intended commercialization efforts.

Many bioinformatics and pharma AI inventions are used to identify biomarkers indicative of a disease state, or drugs and/or other regimens to treat particular diseases in certain patients. While the outputs of an innovative algorithm (e.g., the identified drug or biomarker panel) may be marketed and commercialized (and sometimes are themselves patentable), the underlying algorithms are usually not made public. An applicant should ask whether a competitor can realistically gain insight into their algorithmic analysis based on released products. Sometimes patenting the algorithm makes sense, such as when the inventors will be publishing their methodology anyway, or if certain aspects of the algorithm are public-facing. But some algorithms are better left as trade secrets, if such secrets can be kept.

An applicant should also ask whether they will actually be able to detect infringement by a competitor. If a competitor commercializes a biomarker panel, for example, is it possible to identify or reverse-engineer the back-end algorithmic model used to select that panel? If a competitor commercializes a diagnostic test to predict disease state, is it possible to determine what models are being used to output a predictive score or guarantee the accuracy of that score?

Both these analyses should also consider whether regulatory disclosures – both in the US and internationally – or expected advances in reverse engineering over the life of the patent might change the answer.

### 2. How do I patent a black box? And other 112 issues

The diagnostics industry, where much innovation involves big data analysis, image analysis, and pattern recognition, is increasingly turning to machine learning tools to improve the accuracy and resolution of their diagnoses and outputs. But unless the machine learning tools use explainable AI, the inner workings of the engine and the classification parameters considered distinctive may not be known. Additionally, because machine learning engines learn differently based on different inputs, there are questions as to whether the outcomes can be repeated with different machines.

As the PTO and courts start to shift more attention to §112 issues, applicants should consider adding as much detail and as many examples as they can to the application as filed, so that the disclosure can meet the law as it evolves. Some ways to mitigate potential 112 concerns involve deeply detailed disclosures – identifying specific classes of machine learning models and neural networks, clearly specifying model inputs, and potentially even providing sample sets of data that can be used by a person of skill in the art to build or train a model covered by the invention.

### 3. Is the invention patent eligible?

Bioinformatics innovation gets caught between a rock and a hard place when it comes to current eligibility jurisprudence. Eligibility issues in the life sciences have traditionally involved the naturally occurring subject matter exception; eligibility issues in software have mainly involved the abstract idea exception. Present-day diagnostics and pharma AI must navigate between both.

There have not been many Federal Circuit decisions related to bioinformatics technology. The most relevant are the Stanford cases[1], which issued from the Federal Circuit in March and April of 2021. Stanford had claimed improvements to the field of haplotype phasing by (1) increasing the accuracy of haplotype prediction using a Hidden Markov Model (HMM), a specific machine learning techniques; and (2) by identifying a greater number of haplotype phases based on additional data, such as linkage disequilibrium and transition probability data. The claims described the data input to the HMM, and identified the expected output. Stanford was able to show that the new model correctly identified haplotype phase for 97.9% of all heterozygous positions, compared to about 80% using previous models.

Because the invention focused on the mathematical models, however, the Federal Circuit agreed with the USPTO that the claims merely recited an abstract mathematical concept without significantly more. The last step of each claim recited outputting the haplotype phase result. While such output was itself very useful to patients and clinicians in

[1] *In Re Board of Trustees of the Leland Stanford Junior University*, No. 20-1288 (Fed. Cir. 2021);

*In Re Board of Trustees of the Leland Stanford Junior University*, No. 20-1012 (Fed. Cir. 2021).

deciding future care, the output was, nonetheless, just information. While the Federal Circuit recognized that the mathematics were improved, and that there was an improvement in the resultant data, they concluded that the fundamental operation of the computer was unchanged – the computer merely executed the mathematical algorithm (however novel it might be) to generate the result.

The Federal Circuit did leave some openings for future bioinformatics applicants – they noted that Stanford had other arguments related to improvements in the computer's efficiency, but did not timely raise the arguments so they were not considered. If an applicant can show that the algorithmic changes result in improvements to the computer's efficiency, storage, speed, etc., the applicant's "practical application" arguments might succeed where Stanford's did not.

But what the future holds for eligibility is currently fuzzy. In a world where serious decisions are made based on the accuracy of diagnostic results, and where health innovation is advanced by the discovery of correlations between previously unknown genotypes and phenotypes, it is troubling to many applicants that there are such challenges in proving that this type of innovation is worthy of patent protection.

### 4. *Vanda* and divided infringement

One escape route out of the eligibility morass for pharma AI and bioinformatics is to claim a treatment step, where the results of the computational analysis are used to treat a patient identified as having a particular condition or disease.[2]

For many diagnostic companies, though, the innovation relates to how the patient is diagnosed with a disease in the first place, or how the drug's efficacy is initially discovered – not the ultimate treatment step. Complicating matters further, the companies performing the diagnostic computational analysis are often separate from the clinician administering the treatment. Applicants pursuing this "treatment step" route must be careful not to introduce divided infringement issues into their claims, such that no single entity is likely to ever infringe the claim. Instead, it may be prudent to draft the claim from the perspective of the clinician, whose patient has been identified as having a disease using the diagnostic method, rather than positively claiming the diagnostic method itself. Then, there is likely to at least be a single infringer, even if the patentee then may be faced with a choice between enforcement against a clinician and developing an inducement or contributory infringement case against its true competitor.

### 5. Silicon Valley culture clash

The pharmaceutical and diagnostics industries have traditionally been proponents of a robust, innovator-centric patent system. Inventors employed by most life sciences companies tend to cooperate with their IP counsel, and are frequently involved in the patent process. By comparison, many software/AI developers have a very different view of the patent system,

[2] *Vanda Pharmaceuticals Inc. v. West-Ward Pharmaceuticals*, 887 F.3d 1117 (Fed. Cir. 2018).

and see patents as a hindrance to innovation and speed of development. Life sciences companies whose legal teams come from a life sciences background can be surprised by the skepticism with which their traditional IP strategies are met by software developers who now form an integral part of their innovation team. Also, patenting strategies traditionally implemented by life sciences companies may not make sense with fast-moving and quickly outdated software innovation.

One way to mitigate this IP culture clash includes bringing software IP professionals onto the legal teams at traditional life sciences companies. Additionally, it is important to ensure that new developers understand the product cycle and competitive landscape for pharmaceuticals – and that the legal team understands the domestic and international challenges related to patenting software. Providing infrastructure and policies for submitting disclosures and holding training sessions for AI inventors to recognize when their work constitutes patentable innovation can also ease this cross-disciplinary integration.

### 6. Open source commitments

The proliferation of software tools for machine learning or deep learning means that developers do not need to build all their models from the ground up – they can instead use known, tested models as the foundation for implementing their innovation. Open source (OS) repositories present a wealth of code to assist in this endeavor, but also present traps for the unwary. This is because most OS software grants use under particular licenses, which are selected by the original author and which contain a variety of limitations on use by others. Some OS licenses restrict code use to non-commercial activities. Some OS licenses include provisions that limit the filing of IP – particularly patents – on software tools using the OS code. Some OS licenses include a grant-back provision giving the original author unlimited permission to use any derivative work containing the OS code. To make it even more challenging, some OS licenses are completely incompatible with other OS licenses, meaning that serious legal issues can result when a developer mixes code selected from multiple OS trees. Legal teams should ensure their infrastructure permits OS code auditing, and that systems exist for tracking OS usage by their developers.

### 7. Inventorship and Ownership

No discussion of AI patents – in any industry – would be complete without raising a question about inventorship as AI technology gets more and more sophisticated. While many IP offices around the globe have reassured the public that current AI technology does not rise above current inventorship laws (e.g., the DABUS cases), we can foresee a time where sentient AI could challenge the bounds of those laws.

Such a futuristic question of inventorship raises further questions of ownership. Does the AI "brain" need to assign its rights somehow? Or is the output of an AI engine automatically owned by the company who uses the AI engine? Even now, is there any concern caused by companies using the cloud-based, public AI engines and deep learning networks developed and managed by independent tech companies? Knowing that our technology will continue to evolve, stakeholders need to ensure that our patent laws also evolve to meet those advances, not just respond reactively.

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It's clear that the confluence between traditional biopharma and high tech software tools, which use machine learning and predictive algorithms to match the best treatments to the best patients, holds great promise for innovation advancement. This technology merger also brings challenges, as we try to protect innovation where the most valuable outputs are insights and information. As our patent system evolves, we must ensure that cross-disciplinary inventions are not left vulnerable.

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