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# THE STRUGGLING HYPOTHETICAL: PHOSITA IN THE AGE OF AI DRUG DISCOVERY AND DEVELOPMENT

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## ABSTRACT

This Article examines the extent to which recent advances in artificial intelligence drug discovery and development ("AIDD") destabilize the conventional "Person Having Ordinary Skill in the Art" ("PHOSITA") analysis under U.S. patent law. Unlike traditional approaches, AIDD leverages advanced machine learning algorithms and large-scale datasets to vastly augment computational power and automation throughout the drug development pipeline. This technological evolution renders judicial interpretations of the PHOSITA framework increasingly uncertain, risking a distortion of the non-obviousness threshold that may either stifle innovation or compromise public health.

Through interdisciplinary analysis, this Article systematically analyzes how the rapid proliferation of AIDD technologies recalibrates the normative and practical contours of the PHOSITA construct, with particular attention to the evolving level of ordinary skill and creativity attributed to the PHOSITA. It critically evaluates and synthesizes prevailing proposals, categorizing them into: (1) maintenance of the existing framework, (2) moderate adaptation to accommodate artificial intelligence ("AI"), and (3) wholesale replacement of the PHOSITA framework. By exposing doctrinal inconsistencies, technical limitations, and practical deficits within these proposals, this study elucidates the profound tension between the legal orthodoxy of PHOSITA and technological disruption. Ultimately, this Article proposes a dual-track solution: expedient measures within the existing legal framework and a long-term vision, implemented through collaboration between the Food and Drug Administration ("FDA") and the United States Patent and Trademark Office ("USPTO"), to supplant non-obviousness with the inventive commercial viability standard. These proposals aim to reconcile patent law's innovation mandate with the imperatives of public health.

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## I. INTRODUCTION

In recent years, AI has ushered in a profound transformation in pharmaceutical research and development ("R&D").[1] Unlike traditional Computer-Aided Drug Design ("CADD"), which follows fixed algorithmic pathways, AIDD operates on a data-driven paradigm.[2] Equipped with generative and predictive capabilities, AIDD models are capable of independently designing new molecular structures while concurrently forecasting predictive proxies for efficacy and safety, such

1. WELLCOME TRUST & BOSTON CONSULTING GROUP, UNLOCKING THE POTENTIAL OF AI IN DRUG DISCOVERY 6 (2023).
2. Anastasiia V. Sadybekov & Vsevolod Katritch, *Computational Approaches Streamlining Drug Discovery*, 616 NATURE 673, 678 (2023).

as target potency, selectivity, clearance and permeability.[3] With these advancements, AIDD substantially reduces the need for human intervention in early-stage drug development.

This Article focuses on a fundamental doctrinal uncertainty brought about by AIDD — namely, how to construct the hypothetical PHOSITA in the context of pharmaceutical patents under U.S. patent law. While the PHOSITA framework has long been at the core of the non-obviousness analysis,[4] it has become increasingly unstable amid the rise of interdisciplinary research.[5] Crucially, such uncertainties are amplified in the era of AIDD. In *AliveCor, Inc. v. Apple Inc.*,[6] the Federal Circuit explicitly endorsed a view of the PHOSITA that incorporates access to machine learning algorithms, thereby bringing even more uncertainties into the analytical structure of the PHOSITA.[7] First, AIDD complicates the determination of the pertinent art(s), as inventive processes increasingly embody and reflect cross-disciplinary collaboration, blurring traditional boundaries between chemistry, biology, and AI. Second, it destabilizes the assessment of the level of skill, as the opacity of underlying models and training data, as well as the insufficient explainability and reproducibility of AIDD systems, makes it inherently difficult to identify what constitutes an "average" or representative model that the PHOSITA might reasonably be expected to use. Lastly, it aggravates the difficulty of reasonably estimating ordinary creativity, especially when courts must account for the PHOSITA's capability to tweak and tune AIDD models and select datasets for training. Collectively, these disruptions render the conventional PHOSITA construct increasingly difficult to apply in a principled or predictable manner. The resulting doctrinal instability threatens to distort the non-obviousness analysis in new chemical entity ("NCE," also known as active pharmaceutical ingredient) patent cases, where accurate assessment is especially vital, as these patents serve as a critical safeguard for both innovation incentives and public health access.[8]

To tackle this challenge, a number of scholars and practitioners have already proposed solutions. These proposals can be broadly categorized into three approaches: (1) status quo approaches that rely on the current PHOSITA framework's doctrinal flexibility, (2) reformist proposals that recommend adjustments to the characterization of either the "person" or the "skill" within the PHOSITA construct, and (3) replacement models that seek to marginalize the PHOSITA through

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3. *See infra* text accompanying note 48.

4. Dan L. Burk, *Biotechnology in the Federal Circuit: A Clockwork Lemon*, 46 ARIZ. L. REV. 441, 454 (2004).

5. Dan Traficonte & Ben Armstrong, *People Having Ordinary Skills in the Arts*, 37 HARV. J. L. & TECH. 329, 334 (2024).

6. 130 F.4th 1006 (Fed. Cir. 2025).

7. *Id.* at 1015.

8. *See infra* text accompanying note 114.

alternative objective benchmarks that are based on the facts before or after the inventive process.[9] While each proposal offers valuable insights, they collectively face persistent limitations, such as underestimating the analytical complexities involved in constructing a PHOSITA with access to AIDD tools, inadequately reducing the doctrinal influence of the PHOSITA in the non-obviousness analysis, and conflicting with existing patent law doctrines.

With these in mind, there are several expedient measures that operate within the existing non-obviousness framework, including strategies such as relying on new targets and unexpected improvements on other properties. While these approaches offer short-term doctrinal utility, they are ultimately contingent on the capabilities of AIDD technologies and cannot serve as a sustainable basis for patentability analysis. Recognizing the doctrinal and functional limits of these interim strategies, this Article advances a more structural solution. It proposes replacing non-obviousness with a new standard — inventive commercial viability — which integrates both technical inventiveness and commercial viability. This framework is designed to realign patent doctrine with the goals of incentivizing meaningful pharmaceutical innovation and promoting public health. A concrete implementation pathway requires coordinated FDA-USPTO engagement, in which the FDA serves as a technical assessor through a dedicated fast-track initiative for AIDD inventions, while the USPTO retains its role as the final legal decision-maker on patentability. This is followed by a defense of the proposal's doctrinal legitimacy.

This Article proceeds as follows: Part II outlines the technological evolution of AIDD and its inherent limitations. Part III demonstrates the analytical framework for constructing the PHOSITA and explains how AIDD technologies complicate this inquiry. Part IV critically reviews existing proposals. Part V elaborates on the recommended framework and addresses its potential limitations, followed by a brief conclusion.

## II. TECHNOLOGICAL BACKGROUND

Pharmaceutical R&D is roughly divided into two phases: drug discovery and drug development. These phases have long involved immense costs, protracted timelines, and high attrition rates.[10] Depending on the therapeutic area and data sources, an investigation suggests that the R&D cost for a new drug ranges from $314 million to $4.46

9. *See infra* Part IV.

10. *See generally* David H. Freedman, *Hunting for New Drugs with AI*, 576 NATURE S50, S50 (2019).

billion.[11] A report by Pharmaceutical Research and Manufacturers of America ("PhRMA") suggests that, on average, developing a new medicine takes ten to fifteen years and costs $2.6 billion, accompanied by plenty of failures — only twelve percent of the candidates that enter clinical trials could eventually receive U.S. regulatory approval.[12] In response to these challenges, scientists developed a series of tools to accelerate drug discovery and development and reduce cost, including high-throughput screening, protein engineering, target-based screening, combinatorial chemistry and molecular library design, and increasingly in recent years, AI-driven methods such as multi-omics target identification, structure prediction (e.g., AlphaFold), machine-learning virtual screening, and *de novo* molecule design.[13] While traditional computational techniques have been employed for decades to mitigate these challenges,[14] the advent of AIDD ushers in a phase of unprecedented advancement for its extensive adoption of deep learning.[15]

To establish the technological context for the subsequent legal analysis, this Part first introduces the process of pharmaceutical R&D, along with the associated patent prosecution and regulatory activities, before outlining traditional CADD to establish a baseline understanding of computational methods. It then charts AIDD's evolution, detailing its core methods, transformative impacts, and key characteristics like its data-driven autonomy. Crucially, it examines AIDD's inherent challenges and limitations, such as lack of interpretability and reproducibility.

### *A. Drug Discovery and Development: A Process Intertwined with Patenting and Regulatory Activities*

Conventional accounts delineate the distinction between drug discovery and drug development at the completion of candidate molecule nomination and the initiation of preclinical studies.[16] Under this

11. Aylin Sertkaya, Trinidad Beleche, Amber Jessup & Benjamin D. Sommers, *Costs of Drug Development and Research and Development Intensity in the US, 2000–2018*, 7 JAMA NETWORK OPEN 2, 2 (2024).

12. *See Research and Development Policy Framework*, PHRMA (Sep. 2024), https://phrma.org/policy-issues/research-development [https://perma.cc/SQP9-QTUF].

13. *See generally* Divya Vemula, Perka Jayasurya, Varthiya Sushmitha, Yethirajula Naveen Kumar & Vasundhra Bhandari, *CADD, AI and ML in Drug Discovery: A Comprehensive Review*, 181 EUR. J. PHARM. SCIS. 106324, 106327, 106336 (2023).

14. *See* Keran Wang, Yanwen Huang, Yan Wang, Qidong You & Lei Wang, *Recent Advances from Computer-Aided Drug Design to Artificial Intelligence Drug Design*, 15 RSC MED. CHEMISTRY 3978, 3978 (2024).

15. *See* Mohit Pandey, Michael Fernandez, Francesco Gentile, Olexandr Isayev, Alexander Tropsha, Abraham C. Stern, Artem Cherkasov et al. *The Transformational Role of GPU Computing and Deep Learning in Drug Discovery*, 4 NATURE MACH. INTEL. 211, 211 (2022).

16. *See Step 1: Discovery and Development*, U.S. FOOD & DRUG ADMIN. (Jan. 4, 2018), https://www.fda.gov/patients/drug-development-process/step-1-discovery-and-development [https://perma.cc/B8DY-LE75].

framework, once a promising candidate molecule is identified, the drug discovery phase concludes and advances into comprehensive preclinical evaluation. This temporal boundary reflects not only scientific workflow but also the evolving landscape of patenting and regulatory oversight throughout the pharmaceutical innovation process.

Drug discovery marks the commencement of pharmaceutical R&D. This phase comprises therapeutic target identification and validation, high-throughput or virtual screening of vast compound libraries, medicinal chemistry optimization, and ultimately, selection of one or more lead candidates with favorable potency, selectivity, and drug-like properties.[17] Once a structurally novel and biologically active compound is identified, patent applications typically embodying composition-of-matter or method-of-use claims are usually filed to secure intellectual property rights and priority dates even before preclinical research begins.[18]

Under the FDA's framework, drug development begins immediately after candidate nomination and includes both preclinical studies and clinical trials. Before initiating human trials, sponsors must conduct laboratory or animal testing to assess absorption, distribution, metabolism, excretion, toxicity ("ADMET") parameters, optimal formulation, and dosing regimens, as well as comparative efficacy and potential treatment interactions.[19] Based on these studies, sponsors then prepare and submit an Investigational New Drug ("IND") application to establish the safety and efficacy of the drug for initiating clinical trials.[20] If successful, sponsors will be required to conduct Phase I–III human studies before receiving marketing approval.[21] During this stage, patent strategy evolves to include steps such as refinement of claims and supplemental filings based on data obtained from experiments conducted after patent filing.

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17. *Id.*

18. *See Maximizing Pharmaceutical Patent Longevity: A Mechanistic and Strategic Guide to IP Term Extension and Lifecycle Fortification*, DRUGPATENTWATCH (Jan. 18, 2026), https://www.drugpatentwatch.com/blog/how-long-do-drug-patents-last/ [https://perma.cc/2XY9-UWY7].

19. *See Step 1: Discovery and Development*, *supra* note 16; *Step 2: Preclinical Research*, U.S. FOOD & DRUG ADMIN. (Jan. 4, 2018), https://www.fda.gov/patients/drug-development-process/step-2-preclinical-research [https://perma.cc/J5HU-EXWA].

20. 21 C.F.R. § 312.22(a) ("FDA's primary objectives in reviewing an IND are, in all phases of the investigation, to assure the safety and rights of subjects, and, in Phase 2 and 3, to help assure that the quality of the scientific evaluation of drugs is adequate to permit an evaluation of the drug's effectiveness and safety.").

21. *Step 3: Clinical Research*, U.S. FOOD & DRUG ADMIN. (Jan. 4, 2018), https://www.fda.gov/patients/drug-development-process/step-3-clinical-research [https://perma.cc/L779-D7S5].

### *B. Traditional CADD Approaches and Their Limitations*

Traditional CADD supports tasks in early-stage drug discovery, ranging from target identification to lead optimization.[22] CADD typically embodies two main approaches: Structure-Based Drug Design ("SBDD") and Ligand-Based Drug Design ("LBDD"). The choice depends on data availability of three-dimensional ("3D") structures of biological targets or ligands.

When the 3D structures of biological targets are available, SBDD can leverage structural information of biological targets to rationally design ligands with optimized binding affinity and specificity, employing computational analysis of molecular interactions and iterative experimental refinement for therapeutic development.[23] By contrast, if 3D structural data is insufficient while ligand data is comparatively abundant, LBDD can be utilized as an alternative strategy. It relies on the structural and physicochemical properties of known ligands to establish quantitative structure-activity relationships ("QSARs"), enabling the prediction and optimization of novel compounds with enhanced biological activity.[24]

Moving on to drug development, traditional CADD contributes to ADMET prediction, albeit still lacking significant contributions to improving predictive capacity. Normally, relevant approaches may include physiologically based pharmacokinetic ("PBPK") and pharmacodynamics ("PD") modeling, which are useful for predicting ADMET parameters.[25] Specifically, the separately conducted PBPK modeling, together with PD modeling, can empower CADD via reverse translation, using simulations to optimize molecular design in pursuit

22. *See* Stephani Joy Y. Macalino, Vijayakumar Gosu, Sunhye Hong & Sun Choi, *Role of Computer-Aided Drug Design in Modern Drug Discovery*, 38 ARCHIVES PHARMACAL RSCH. 1686, 1696 (2022) ("Certainly, the incorporation of computational drug design methods in any stage of the drug discovery process allows great information evolution that can lead to better and more desirable drug candidates.").

23. *See* Leonardo G. Ferreira, Ricardo N. dos Santos, Glaucius Oliva & Adriano D. Andricopulo, *Molecular Docking and Structure-Based Drug Design Strategies*, 20 MOLECULES 13384, 13385–86 (2015) (noting that SBDD involves a cyclical workflow where computer modeling and lab experiments are alternated to design, synthesize, and optimize molecules based on their structure and experimental performance, thus steadily improving binding and therapeutic potential).

24. *See* Jihyun Shim & Alexander D. MacKerell Jr., *Computational Ligand-Based Rational Design: Role of Conformational Sampling and Force Fields in Model Development*, 2 MEDCHEMCOMM 356, 356 (2011).

25. *See* Fengxu Wu, Yuquan Zhou, Langhui Li, Xianhuan Shen, Ganying Chen & Xiaoqing Wang, *Computational Approaches in Preclinical Studies on Drug Discovery and Development*, FRONTIERS CHEMISTRY, Sep. 10, 2020, at 1, 7 (noting that CADD methods, such as QSAR modeling, provide key drug-specific parameters, including volume of distribution, clearance, and permeability, to support PBPK modeling).

of the best integration of multiple parameters.[26] However, there has not been significant progress.

Traditional CADD approaches have already reduced costs and expedited the drug R&D process.[27] Nevertheless, several persistent technical bottlenecks constrain CADD's full potential. Primarily, traditional techniques strictly abide by rigid and manually coded software procedures that operate in a narrowly programmed and mechanistic fashion.[28] These techniques are essentially an extension of manual tasks performed by humans and lack autonomy. Consequently, these techniques are inadequate for scenarios involving complex biological systems, accurately representing target flexibility, or transcending the existing chemical space.[29] Due to this inherent limitation, traditional CADD approaches remain constrained in accuracy, adaptability, and innovative capacity, even if more data becomes available. Therefore, researchers still need to laboriously verify the outcomes yielded by traditional CADD techniques.[30]

### *C. Emergence and Evolution of AI Drug Discovery and Development*

Recent advances in AI, particularly in machine learning and deep learning, are gradually overcoming the above-mentioned technical

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26. *See* Panagiotis Zagaliotis, Anthi Petrou, George A. Mystridis, Athina Geronikaki, Ioannis S. Vizirianakis & Thomas J. Walsh, *Developing New Treatments for COVID-19 through Dual-Action Antiviral/Anti-Inflammatory Small Molecules and Physiologically Based Pharmacokinetic Modeling*, INT'L J. MOLECULAR SCIS., July 20, 2022, at 1, 17 (explaining that integrating PBPK and PD modeling with CADD allows researchers to use simulation results to repeatedly improve and adjust drug molecule designs, so that multiple properties — such as pharmacokinetics, pharmacodynamics, and ADME — can be optimized together during drug development).

27. *See generally* Vemula et al., *supra* note 13.

28. *See, e.g.*, Wang et al., *supra* note 14, at 3979–80 (noting that traditional CADD techniques rely on manually coded software programs for specific, narrowly defined tasks, in contrast to the autonomous learning and flexible execution of AI-based methods).

29. Kampanart Huanbutta, Kanokporn Burapapadh, Pakorn Kraisit, Pornsak Sriamornsak, Thittaporn Ganokratanaa, Kittipat Suwanpitak et al., *Artificial Intelligence-Driven Pharmaceutical Industry: A Paradigm Shift in Drug Discovery, Formulation Development, Manufacturing, Quality Control, and Post-Market Surveillance*, EUR. J. PHARM. SCIS., Oct. 16, 2024, at 1, 3.

30. *See, e.g.*, Brian J. Bender, Stefan Gahbauer, Andreas Luttens, Jiankun Lyu, Chase M. Webb, Reed M. Stein et al., *A Practical Guide to Large-Scale Docking*, 16 NATURE PROTOCOLS 4799, 4800 (2021) (explaining that because SBDD must trade chemical accuracy for computational speed by undersampling conformations, ignoring and simplifying interaction terms, its scoring is inherently error-prone and cannot reliably rank large libraries, necessitating experimental validation); Jianping Huang & Xiaohui Fan, *Why QSAR Fails: An Empirical Evaluation Using Conventional Computational Approach*, 8 MOLECULAR PHARMS. 600, 600–01, 607 (2011) (explaining that QSAR results are often unreliable because of unstable feature selection, the existence of many equivalent but mechanistically distinct models, insufficient external validation, descriptor redundancy, data quality and distribution issues, and chance correlation, all of which undermine the true predictability of QSAR models).

barriers in drug R&D. This Article refers to such techniques as AIDD,[31] a term that reflects AI's central role across the entire process.

1. Technical Foundations of AIDD Models

At the technical level, the foundational principles and frameworks of AIDD differ markedly from that of traditional CADD techniques.[32] An AIDD model typically consists of three components: model configurations, training data, and model parameters. These components impact model performance to varying extent and in different ways. Scientists and developers explicitly define configurations and deliberately select datasets ex ante. Together, they shape the model parameters, which are iteratively updated during training. During this process, the dataset determines what the model learns, the model configurations determine how it learns, and the resulting model parameters encode the learned statistical patterns that allow the model to generate information based on user prompts.

Training data is the basis for AIDD model development. Appropriate data is regarded as crucial for building useful AIDD models that excel in making reliable decisions and molecule generation.[33] AIDD's potential cannot be realized if models are not trained on sufficiently high-quality datasets.[34] Depending on the specific work assignment, researchers can input AIDD models with different kinds of datasets, such as chemical structure data, bioactivity and pharmacological data, protein and target data, ADMET data, and clinical data. In the absence of sufficient, representative, and accurate data, even ostensibly sophisticated model configurations cannot output meaningful results that are valuable for further developments.[35]

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31. Some scholars and scientists also refer to AIDD as "AI-driven drug discovery and development," "AI-enabled drug discovery and development," "AI-generated drugs," or "AI-derived drugs." For discussions of AI drug discovery and development and the potential challenges it may incur in patent law, see Matthew Chun, *Artificial Intelligence for Drug Discovery: A New Frontier for Patent Law*, 104 J. PAT. & TRADEMARK OFF. SOC'Y 5, 5 (2024); Francesca Mazzi, *Patentability of AI Generated Drugs*, 4 EUR. PHARM. L. REV. 17, 17 (2020); Olga Gurgula, *AI-Assisted Inventions in the Field of Drug Discovery: Readjusting the Inventive Step Analysis*, 2 INT'L J. SOC. SCI. & PUB. POL'Y 7, 7 (2020); Janet Freilich & Arti K. Rai, *What Patents on AI-Derived Drugs Reveal*, 388 SCI. 924, 924 (2025).

32. Regarding terminology, some scholars also consider AIDD to be a branch of CADD techniques but acknowledge its substantial distinction from traditional CADD techniques.

33. Petra Schneider, W. Patrick Walters, Alleyn T. Plowright, Norman Sieroka, Jennifer Listgarten, Robert A. Goodnow Jr. et al., *Rethinking Drug Design in the Artificial Intelligence Era*, 19 NATURE REVS. DRUG DISCOVERY 353, 353 (2020).

34. Catrin Hasselgren & Tudor I. Oprea, *Artificial Intelligence for Drug Discovery: Are We There Yet?*, 64 ANN. REV. PHARMACOLOGY & TOXICOLOGY 527, 527, 540 (2024) (underscoring that poorly curated, insufficient or unrepresentative datasets may lead to unreliable models and failed predictions).

35. Schneider et al., *supra* note 33, at 353.

Model configurations encompass the architecture, algorithms, and associated hyperparameters, all of which are defined and specified before training and not learned from training data.[36] Normally, model developers select the architecture and algorithms before tuning hyperparameters. The model architecture determines the structure of the model (such as the number and size of neural network layers) and addresses diverse problems in drug discovery by matching the model structure to the nature of the data and the prediction task,[37] with different networks — such as convolutional neural networks ("CNNs"), recurrent neural networks ("RNNs"), and generative adversarial networks ("GANs") — serving distinct functions within the drug discovery and development pipeline.[38] Simultaneously, developers carefully determine algorithms for specifying the learning and optimization procedures (such as supervised learning and optimizer, respectively),[39] and even improving explainability.[40] Upon the determination of the architecture and algorithms, AI scientists and developers then embark on tuning hyperparameters. Hyperparameters (such as learning rate, batch size, and number of epochs) govern some critical training aspects including stability and generalization.[41]

Methodologically, model configurations are imperative because they collectively determine the search space and inductive biases of the model by defining which functions the model can approximate and how efficiently it can be trained and generalized.[42] Therefore, selecting

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36. *See* Li Yang & Abdallah Shami, *On Hyperparameter Optimization of Machine Learning Algorithms: Theory and Practice*, 415 NEUROCOMPUTING 295, 295 (2020).

37. Jessica Vamathevan, Dominic Clark, Paul Czodrowski, Ian Dunham, Edgardo Ferran, George Lee et al., *Applications of Machine Learning in Drug Discovery and Development*, 18 NATURE REVS. DRUG DISCOVERY 463, 466 (2019).

38. *Id.* (explaining that the selection of model architecture is guided by the nature of the data and the specific question addressed in each stage of the pipeline, and that appropriate architecture choice is critical for maximizing model performance and interpretability). The authors also introduced some common neural networks, such as CNNs (extracting hierarchical features from molecular graphs and images), RNNs (model sequential and temporal dependencies in molecular or biological data) and GANs (facilitating the generation of novel chemical structures).

39. Schneider et al., *supra* note 33, at 356 (noting the algorithms for implements an evolving problem-solving heuristic and for training model's predictive capabilities).

40. *See generally* José Jiménez-Luna, Francesca Grisoni & Gisbert Schneider, *Drug Discovery with Explainable Artificial Intelligence*, 2 NATURE MACH. INTEL. 573, 573 (2020).

41. *See* Ali Ebadi, Manpreet Kaur & Qian Liu, *Hyperparameter Optimization and Neural Architecture Search Algorithms for Graph Neural Networks in Cheminformatics*, COMPUTATIONAL MATERIALS SCI., May 20, 2025, at 1, 2 (exemplifying that hyperparameter optimization is indispensable for enhancing training generalizability and stability of GNNs).

42. *See* Luca Franceschi, Michele Donini, Valerio Perrone, Aaron Klein, Cédric Archambeau & Matthias Seeger, *Hyperparameter Optimization in Machine Learning*, 18 FOUNDS. & TRENDS MACH. LEARNING 975, 985, 988 (2024), https://arxiv.org/pdf/2410.22854v1 [https://perma.cc/ZEB2-382V] (noting that an ML model's practical generalization turns on hyperparameters, and that both model composition (including feature extractors or neural network architecture) and the optimization procedure depend on such tunable quantities, which

appropriate configurations is often a prerequisite for achieving strong model performance. Together, these configuration elements define the model's expressivity, training behavior, and optimization characteristics prior to the input of training data.

Model parameters, such as the learnable and tunable weights and biases, are critical determinants of a model's predictive accuracy, as they encode the learned representations that drive the model's performance on training data.[43] Parameters serve as the only internal values that change during training, being iteratively adjusted via multiple approaches to fit training data optimally.[44] This also reflects the data-driven paradigm of AIDD, as model performance constantly evolves depending on data quality. During generation, new chemical structures are produced exclusively by running the fixed architecture populated with these learned parameters.

In brief, in the process of developing an AIDD model, configurations such as architecture, algorithms, and hyperparameters are pre-determined by human scientists and remain fixed. While the configurations and the training data are both integral to crafting an AIDD model, it is the continuously evolving product of their interaction that has a direct impact on what the model generates. A harmonious and coordinated combination of these technical components is essential to a well-functioning AIDD model.[45]

2. AI Boosts Computational Capacity and Integration Across Stages

At the drug discovery stage, AI demonstrates potential for addressing the critical limitations of traditional techniques. While traditional CADD could be encumbered by the scarcity of 3D structural data or ligands, deep learning techniques such as CNNs and GANs are well-placed to mitigate these problems by extensively exploring and exploiting the existing data such as particular forms of molecular strings and

in turn shape the model's effective hypothesis space and inductive biases in learning task-specific patterns).

43. *See generally* Alex Zhavoronkov, Yan A. Ivanenkov, Alex Aliper, Mark S. Veselov, Vladimir A. Aladinskiy & Anastasiya V. Aladinskaya, *Deep Learning Enables Rapid Identification of Potent DDR1 Kinase Inhibitors*, 37 NATURE BIOTECH. 1038, 1038 (2019).

44. *See What Are Model Parameters?*, IBM (May 5, 2025), https://www.ibm.com/think/topics/model-parameters [https://perma.cc/B4CR-VL5E] ("Model parameters are internal to a model and estimated by it during the learning process in response to training data. The model's learning algorithm updates parameter values during training. Parameters control how a model reacts to unseen data — for example, how a predictor model makes predictions post-deployment.").

45. *See* John P. Santa Maria, Yuan Wang & Luiz Miguel Camargo, *Perspective on the Challenges and Opportunities of Accelerating Drug Discovery with Artificial Intelligence*, 3 FRONTIERS BIOINFORMATICS 3, 3 (2023).

sequences of certain protein components.[46] More remarkably, AI significantly enhances CADD by enabling the analysis of vast and complex datasets. Unlike traditional methods, machine learning algorithms can detect hidden patterns and relationships across multiple types of large-scale datasets (such as molecular structures, bioactivity, toxicity, and genomic information) that conventional approaches fail to capture.[47] This allows researchers to uncover insights that would otherwise remain invisible to humans. Simultaneously, multi-objective optimization on a candidate molecule and realization of all-around enhancement of all related parameters have also become possible.[48] Accordingly, AI-driven methods have expanded the analytical reach of drug discovery, enabling more systematic exploration beyond conventional scientific assumptions and extending the chemical space. In practice, AI models can generate and predict the quality of *de novo* molecules that were never synthesized in the real world.[49]

In parallel, unprecedented innovations are surging in drug development. During preclinical trials, digital twins ("DTs") can simulate drug-biological system interactions, ranging from individual cells to animals.[50] Also, these tools can help refine clinical trial design by improving patient selection and eligibility assessment, enhancing

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46. *See generally* Heba Askr, Enas Elgeldawi, Heba Aboul Ella, Yaseen A. M. M. Elshaier, Mamdouh M. Gomaa & Aboul Ella Hassanien, *Deep Learning in Drug Discovery: An Integrative Review and Future Challenges*, 203 A.I. REV. 5975, 5983–92 (2022).

47. Alexandre Blanco-González, Alfonso Cabezón, Alejandro Seco-González, Daniel Conde-Torres, Paula Antelo-Riveiro, Ángel Piñeiro et al., *The Role of AI in Drug Discovery: Challenges, Opportunities, and Strategies*, 16 PHARMACEUTICALS 891, 892–93 (2023) (comparing AIDD with CADD and explaining that AI approaches can analyze large amounts of diverse information to identify patterns not apparent to human researchers, thereby enabling faster and more accurate drug discovery and further exemplifying that AIDD can learn simultaneously from molecular structures, bioactivity, toxicity, and genomic data).

48. Schneider et al., *supra* note 33, at 356 (explaining that AIDD enables multi-objective optimization by using computational predictive models for each desired property and applying multi-objective optimization algorithms to identify molecules that optimally balance conflicting properties, generating a set of solution leads where each represents a different trade-off and no solution can be improved in one property without sacrificing another).

49. Alberto Ocana, Atanasio Pandiella, Cristian Privat, Iván Bravo, Miguel Luengo-Oroz, Eitan Amir et al., *Integrating Artificial Intelligence in Drug Discovery and Early Drug Development: A Transformative Approach*, BIOMARKER RSCH., Mar. 14, 2025, at 1, 6 (explaining that, unlike traditional CADD methods which rely on existing chemical libraries, AIDD can implement de novo drug design by using generative AI models such as GANs, variational auto encoders, and reinforcement learning, thereby enabling the creation of entirely new molecular structures optimized for specific biological properties).

50. Maria Bordukova, Nikita Makarov, Raul Rodriguez-Esteban, Fabian Schmich & Michael P. Menden, *Generative Artificial Intelligence Empowers Digital Twins in Drug Discovery and Clinical Trials*, 19 EXPERT OPINION DRUG DISCOVERY 33, 36 (2023) (noting that digital twins, empowered by generative AI, are being applied at the preclinical stage of drug discovery — from single cells and cell cultures to tissues, organs, and animal models — to enable virtual perturbation experiments, predict drug response, simulate toxicity, and optimize experimental setups, thereby accelerating drug screening and reducing reliance on traditional wet-lab and animal studies).

accuracy and efficiency.[51] After determining initial trial participants, DTs can also simulate clinical trials on participants in virtual space in advance.[52] Scientists have discovered that in some therapeutic areas, DT clinical trials more accurately reflect real-world therapeutic responses, narrowing the discrepancies between preclinical experimental data and clinical efficacy.[53] While current technologies cannot yet fully replicate complex biological systems, steady progress is being made.[54] Notably, companies are increasingly integrating structured and unstructured data to improve predictions of clinical trial success in later development stages,[55] which epitomizes more extensive utilization of available data.

Rising computational power, advanced algorithms, and ample multimodal data are driving multi-level integration in drug R&D. Apart from synergizing research methodologies, AI also enables companies to build end-to-end discovery platforms.[56] On an organizational level, this promotes widespread automation, leading to self-driving laboratories ("SDLs") where robots reduce manual work and directly feed data to AI.[57] Ultimately, such SDLs could empower non-experts,[58] decreasing the involvement of pharmaceutical scientists.

Novel AI techniques overcome the limitations of traditional CADD and demonstrate remarkable autonomy. As noted, AI has gradually

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51. *See* Ocana et al., *supra* note 49, at 8–9 ("AI algorithms can assess patient eligibility more quickly by evaluating electronic health records (EHRs), ensuring suitable candidates are screened for trials.").

52. *Id.* at 9.

53. *See, e.g.*, Chanchala Kaddi, Mengdi Tao, Silke Bergeler, Kelly George, Hugo Geerts, Piet H. van der Graaf et al., *Quantitative Systems Pharmacology-Based Digital Twins Approach Supplements Clinical Trial Data for Enzyme Replacement Therapies in Pompe Disease*, 117 CLINICAL PHARMACOLOGY & THERAPEUTICS 579, 579 (2025) (discussing how DTs may address the scarcity of preclinical experimental data in rare disease research).

54. Hossein Akbarialiabad, Mahdiyeh Sadat Seyyedi, Shahram Paydar, Adrina Habibzadeh, Alireza Haghighi & Joseph C. Kvedar, *Bridging Silicon and Carbon Worlds with Digital Twins and On-Chip Systems in Drug Discovery*, NPJ SYS. BIOLOGY & APPLICATIONS, Dec. 19, 2024, at 1, 2 (noting that "ongoing advancements in the field continue to push the boundaries of what DTs can achieve").

55. *See* Alex Aliper, Roman Kudrin, Daniil Polykovskiy, Petrina Kamya, Elena Tutubalina, Shan Chen et al., *Prediction of Clinical Trials Outcomes Based on Target Choice and Clinical Trial Design with Multi-Modal Artificial Intelligence*, 114 CLINICAL PHARMACOLOGY & THERAPEUTICS 972, 973 (2023) (noting that companies are increasingly integrating structured data — such as omics, trial attributes, and chemical properties — and unstructured data from sources like press releases and scientific literature to improve the prediction of clinical trial success in later-stage drug development).

56. *See generally* Jiho Yoo, Tae Yong Kim, InSuk Joung & Sang Ok Song, *Industrializing AI/ML During the End-to-End Drug Discovery Process*, CURRENT OP. STRUCTURAL BIOLOGY, Feb. 1, 2023, at 1, 1–2.

57. Roman Kasianov, *Insilico Medicine Raises $110m to Advance AI Drug Design, Unveils Its Humanoid Lab Robot*, BIOPHARMATREND (Mar. 12, 2025), https://www.biopharmatrend.com/post/1162-insilico-medicine-raises-110m-to-advance-ai-drug-design-unveils-its-humanoid-lab-robot/ [https://perma.cc/VZU2-Y82Q].

58. *See generally* Milad Abolhasani & Eugenia Kumacheva, *The Rise of Self-Driving Labs in Chemical and Materials Sciences*, 2 NATURE SYNTHESIS 483, 488–89 (2023).

reduced human intervention in drug R&D and integrated various stages on different levels. The assimilation of AI is a paradigm shift that not only alleviates data scarcity and strengthens processing capabilities, but also blurs the boundaries between previously separated stages and accelerates end-to-end integration. Some practitioners believe that drugs autonomously invented by AI will appear by 2030.[59]

3. AIDD's Limitations and Challenges

Nevertheless, AIDD also introduces novel challenges. Unlike traditional CADD methods, AIDD models lack interpretability and explainability. As self-evolving algorithms become increasingly complex, they offer limited transparency, leading to mistrust in their outputs.[60] At the same time, AIDD models are characterized by sensitivity. As mentioned, the parameters of AIDD models are collectively shaped by unchanged factors such as architecture, algorithms, hyperparameters, and the constant inflow of training data.[61] Scientists suggest that even minor revisions to configurations or inputting small datasets for fine-tuning may have a significant impact on model performance.[62] Furthermore, AIDD's data-driven nature implies demand for high-quality multimodal training data. Low-quality data and imbalanced public databases remain a major challenge, underscoring the urgent

59. *See, e.g.*, Corey A. Salsberg, *AI and the Bio-Pharmaceutical Sector*, WIPO AI & IP DIALOGUES, at 2:44:49 (Sep. 21, 2022), https://webcast.wipo.int/video/WIPO_IP_CONV_GE_2_2022-09-21_AM_116688 [https://perma.cc/SWP5-559W].

60. *See* Askr et al., *supra* note 46, at 6011.

61. *See infra* Section II.C.1.

62. Such impacts can be positive or negative. In the era of AIDD, this weighs heavily on subsequent determinations of the level of skill in the art and ordinary creativity. *See, e.g.*, Xiangxiang Zeng, Hongxin Xiang, Linhui Yu, Jianmin Wang, Kenli Li, Ruth Nussinov et al., *Accurate Prediction of Molecular Properties and Drug Targets Using a Self-Supervised Image Representation Learning Framework*, 4 NATURE MACH. INTEL. 1004, 1005 (2022) (noting that the choice of model architecture or algorithm has a substantial impact on AIDD performance, as demonstrated by systematic comparisons showing significant differences in predictive accuracy among various models); *id*. at 1010–11 (noting that changing hyperparameters can significantly affect model performance, as demonstrated by experiments showing that different hyperparameter settings result in measurable differences in accuracy and robustness); Joren Van Herck, María Victoria Gil, Kevin Maik Jablonka, Alex Abrudan, Andy S. Anker, Mehrdad Asgari et al., *Assessment of Fine-Tuned Large Language Models for Real-World Chemistry and Material Science Applications*, 16 CHEM. SCI. 670, 672 (2025) (noting that minor modifications to the architecture or hyperparameters of AI models, such as the number of fine-tuning epochs, can significantly affect the predictive performance of AIDD models); Laura Isigkeit, Tim Hörmann, Espen Schallmayer, Katharina Scholz, Felix F. Lillich & Johanna H. M. Ehrler, *Automated Design of Multi-Target Ligands by Generative Deep Learning*, NATURE COMMC'NS, Sep. 11, 2024, at 1, 3 (noting that different fine-tuning strategies may rapidly erase the model's learned similarity to previously targeted ligands or cause the model's focus to "flip" between targets); *id*. at 6 (stating that alternating fine-tuning strategies seemingly disrupted the model, resulting in instability and a lack of balanced learning across multiple targets).

need for effective data curation.[63] Consequently, even subtle variations in model configurations or training datasets can result in pronounced discrepancies in model parameters, impacting the model's eventual performance.

In addition, concerns with reproducibility further compound these challenges. Scholars such as Hasselgren and Oprea have highlighted the difficulty of consistently verifying the claimed therapeutic effects of the molecules generated by AIDD models.[64] Due to the inherent stochasticity of machine learning, even identical input data may yield varying outputs, exacerbating uncertainty and undermining confidence in AIDD results.[65] This also has implications for model evaluation. Even with fixed parameters and identical instructions, the same model often produces highly variable outputs, rendering the appraisal of the model even more arduous. All these technical challenges, together with the characteristics of AIDD, can lead to difficulties in the legal analysis of the PHOSITA.

## III. THE STRUGGLING PHOSITA: TREMENDOUS UNCERTAINTIES

Despite AIDD's transformative benefits across R&D stages, it also gives rise to pressing legal challenges, particularly in the domain of patent law. Among these, the non-obviousness analysis in pharmaceutical inventions has become increasingly fraught with complexity. At the heart of this tension lies the construct of the PHOSITA, which serves as a legal agent for evaluating obviousness. Pursuant to 35 U.S.C. § 103 ("Section 103"), an invention shall not be patented if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious to a PHOSITA[66] before the effective filing date.[67] In *Graham*, the Supreme Court identified the following inquiries for evaluating obviousness: (1) determining the scope and content of the prior art, (2) ascertaining the differences between the claimed invention and the prior art, and (3) resolving the level of ordinary skill in the pertinent art(s).[68] In addition to these factors, the Court listed objective indicia, also known as

63. Vemula et al., *supra* note 13, at 19.

64. Hasselgren & Oprea, *supra* note 34, at 541.

65. Vamathevan et al., *supra* note 37, at 474.

66. In other jurisdictions, such as the UK and the signatories to the European Patent Convention, it is also known as "POSITA," "POSA," or "PSA." Some U.S. scholars and judges also refer to it as the "skilled artisan," "skilled person," or "notional person."

67. 35 U.S.C. § 103 ("A patent for a claimed invention may not be obtained . . . if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains.").

68. Graham v. John Deere Co., 383 U.S. 1, 17 (1966).

"secondary considerations," that the USPTO needs to evaluate on a case-by-case basis, including (1) evidence of commercial success, (2) long-felt but unsolved needs, (3) failure of others, and (4) unexpected results.[69] In accordance with Section 103, the analysis of both primary and secondary considerations will eventually be interpreted from the perspective of the PHOSITA.[70]

This Part is divided into two Sections. Section III.A provides a systematic account of how U.S. patent law doctrinally constructs the PHOSITA in pharmaceutical cases, focusing on its three constituent elements: the pertinent art(s), the level of ordinary skill, and the degree of creativity. Section III.B then examines how the advent of AIDD technologies disrupts each of these elements, introducing significant uncertainties into the non-obviousness analysis.

### *A. The Legal Framework of the PHOSITA in the Pharmaceutical Industry*

Under the current U.S. patent law regime, the PHOSITA is supposed to play a central role in guiding the non-obviousness inquiry.[71] The construction of the PHOSITA in a given case can be logically broken down into the following steps: (1) determining the pertinent art(s), (2) construing the skill level of the PHOSITA, and (3) estimating the degree of creativity exercised by the PHOSITA.[72]

#### 1. Determining the Pertinent Art(s)

Initially, examiners and judges must determine the art(s) in which the PHOSITA specializes. According to the Manual of Patent Examining Procedure ("MPEP"), the identification of the art(s) begins with a comprehensive understanding of the disclosed invention in the patent application, including reading the claims and the specification.[73] The analysis must adopt the "broadest reasonable construction in light of the specification."[74] Therefore, in principle, the analysis of the pertinent art(s) should be open to extensive interpretation. Some scholars even contend that the Supreme Court took a fairly broad view that permitted the discussion of any discipline in patent cases.[75] Furthermore,

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69. *Id.*; MPEP § 2141(II) (9th ed. Rev. 01.2024, Nov. 2024).

70. *See* 35 U.S.C. § 103, *supra* note 67.

71. *See* Laura Pedraza-Farina & Ryan Whalen, *The Ghost in the Patent System: An Empirical Study of Patent Law's Elusive "Skilled Artisan,"* 108 IOWA L. REV. 247, 258 (2022).

72. *See* Traficonte & Armstrong, *supra* note 5, at 340.

73. MPEP § 2141(II)(A) (9th ed. Rev. 01.2024, Nov. 2024).

74. Phillips v. AWH Corp., 415 F.3d 1303, 1316 (Fed. Cir. 2005) (citation modified).

75. *See e.g.*, Laura G. Pedraza-Farina, *Patent Law and the Sociology of Innovation*, 2013 WIS. L. REV. 813, 862 (2013) (characterizing the Court's holding in KSR Int'l Co. v. Teleflex

where parties disagree on the specialization of the PHOSITA, the account of the inventors retrieved from the patent application can be taken into consideration. For example, in *Daiichi Sankyo Co., Ltd. v. Apotex, Inc.*,[76] the Federal Circuit held that the PHOSITA should be a specialist rather than a generalist professional in light of the field of specialization of the inventors as recorded on the patent application.[77]

In practice, opposing parties usually adopt varying approaches to delineating the scope of the pertinent art(s) in light of their own interests.[78] Usually, as the parties' briefings in *Daiichi Pharm. Co. v. Apotex, Inc.*[79] demonstrate, the challenging parties would prefer a narrower scope and argue that the PHOSITA possesses considerable skill and creativity in the specialized area to increase the chance of finding the claimed invention obvious.[80] However, sometimes the patent owner may also argue in favor of a specialist PHOSITA to prevent detrimental references from being considered by judges.[81] Likewise, depending on the facts of the case, parties may, for their own interests, demonstrate divergent views regarding the pertinent art(s) that the PHOSITA focuses on, particularly when the claimed invention involves multi-disciplinary collaboration in disparate technical fields that have been previously rarely integrated.

When it comes to the perspective of judges, one empirical study on court judgments finds no significantly more in-depth analysis that discusses the PHOSITA in cases that involve distant and non-proximate technical fields compared with cases that involve highly proximate technical fields.[82] Another empirical study suggests that such lack of analysis of a multi-disciplinary PHOSITA may be due to the lack of interdisciplinarity in the field of the invention at the relevant time.[83]

Once the relevant arts are determined, the PHOSITA is presumed to have knowledge about all prior art references in these fields, which is clearly different from how an actual inventor with ultimately limited

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Inc., 550 U.S. 398, 420 (2007), as "[i]f there is a problem to be solved . . . a PHOSITA would use all tools available, from any discipline, to solve it.").

76. 501 F.3d 1254 (Fed. Cir. 2007).

77. *See id.* at 1257.

78. Rebecca S. Eisenberg, *Obvious to Whom? Evaluating Inventions from the Perspective of PHOSITA*, 19 BERKELEY TECH. L.J. 885, 899 (2004) (explaining that, given the high stakes of litigation, each party advances conflicting expert accounts of obviousness, leading to polarized and potentially distorted reconstructions of the PHOSITA perspective).

79. 380 F. Supp. 2d 478 (D.N.J. 2005).

80. *See id.* at 484.

81. *See, e.g.*, Axonics, Inc. v. Medtronic, Inc., 73 F.4th 950, 955 (Fed. Cir. 2023).

82. Pedraza-Farina & Whalen, *supra* note 71, at 276.

83. *See* Saurabh Vishnubhakat & Arti K. Rai, *When Biopharma Meets Software: Bioinformatics at the Patent Office*, 29 HARV. J.L. & TECH. 205, 237–39 (2015).

cognitive capacity behaves.[84] The prior art is limited to the references that came into existence before the effective filing date of the claimed invention.[85] However, it does not cover confidential internal documents that are not supposed to be publicly accessible.[86] Specifically, public accessibility cannot be established if there exists a reasonable expectation of confidentiality.[87] For this reason, confidential proprietary databases under control of research institutes or private corporations legally cannot be regarded as prior art.

2. Determining the Skill Level of the PHOSITA

The PHOSITA's skill in the art should be ordinary, not the one of the inventor, "a judge, . . . a layman, . . . those skilled in remote arts, or . . . geniuses in the art at hand."[88] The PHOSITA has knowledge of scientific and engineering principles in the pertinent art(s).[89] The Federal Circuit has provided a series of non-exhaustive factors for ascertaining the level of ordinary skill, namely, (1) the "type[s] of problems encountered in the art," (2) the "prior art solutions to those problems," (3) the "rapidity with which innovations are made," (4) the "sophistication of the technology," and (5) the "educational level of active workers in the field."[90]

Despite the lack of a direct reference,[91] examiners and judges have generally factored in access to toolkits or equipment. For example, in *In re Kubin*,[92] the Federal Circuit emphasized the availability of the "well-known and reliable nature" of certain laboratory techniques in the prior art.[93] Furthermore, the relevant skills are not necessarily limited to a particular field or a specialized area within a particular field.

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84. *See* Custom Accessories, Inc. v. Jeffrey-Allan Indus., 807 F.2d 955, 962 (Fed. Cir. 1986); Dan L. Burk & Mark A. Lemley, *Is Patent Law Technology-Specific?*, 17 BERKELEY TECH. L.J. 1155, 1188 (2002) ("[U]nlike any actual person of skill in the art, the PHOSITA is endowed with knowledge of all of the relevant prior art references.").

85. MPEP § 2141.01 (9th ed. Rev. 01.2024, Nov. 2024).

86. MPEP § 2128.01(III) (9th ed. Rev. 01.2024, Nov. 2024).

87. *See* Jazz Pharms., Inc. v. Amneal Pharms., LLC, 895 F.3d 1347, 1358–59 (Fed. Cir. 2018).

88. Env't Designs, Ltd. v. Union Oil Co. of Cal., 713 F.2d 693, 697 (Fed. Cir. 1983), *cert. denied*, 464 U.S. 1043 (1984).

89. *Ex parte* Hiyamizu, No. 650-06, 10 U.S.P.Q.2d 1393, 1394 (P.T.A.B. Feb. 8, 1988).

90. *In re* GPAC Inc., 57 F.3d 1573, 1579 (Fed. Cir. 1995).

91. Ryan Abbott, *Everything Is Obvious*, 66 UCLA L. REV. 2, 35 (2019) ("The current standard neglects to appropriately take into account the modern importance of machines in innovation."); Ryan Whalen, *Second-Order Obviousness: How Information and Communication Technologies Make Inventions More Obvious and Why the Law Should Care*, 97 J. PAT. & TRADEMARK OFF. SOC'Y 597, 624–25 (2015) (suggesting that courts' current analysis of the PHOSITA often overlooks the technological tools available to inventors and recommending that judicial instructions explicitly account for such tools and their impact on invention).

92. 561 F.3d 1351 (Fed. Cir. 2009).

93. *Id.* at 1360.

The PHOSITA may also represent a group of individuals that possesses a constellation of skills that are not typically concentrated in any single human being.[94]

In the context of pharmaceutical patent disputes, scholars conclude that the PHOSITA is commonly determined to possess "skills commensurate with an advanced degree (for example, PhD or MD) along with experience in the research or treatment of the specific disease state(s)."[95] Sometimes, judges may acknowledge that a lack of an educational background or work experience in the relevant fields could reciprocally complement each other.[96] In recent cases, some judges have explicitly identified the PHOSITA in pharmaceutical patent disputes as one equipped with the knowledge and experience of a multi-disciplinary team that has familiarity with laboratory techniques and strategies employed in the field.[97] These cases reflect a tendency to construct the PHOSITA in a way that broadly acknowledges its comprehensive expertise in a specific area and its possession of the essential specialized skills of the members in a multi-disciplinary team. The Federal Circuit even found that the PHOSITA in the pharmaceutical field could have certain knowledge in the regulatory rules in a foreign jurisdiction.[98] However, judges may not automatically construe the PHOSITA as having expertise in normally disparate disciplines. Instead, a recent

94. Daralyn J. Durie & Mark A. Lemley, *A Realistic Approach to the Obviousness of Inventions*, 50 WM. & MARY L. REV. 989, 993 (2008).

95. Garth W. Strohbehn, Alec J. Kacew, Daniel A. Goldstein, Robin C. Feldman & Mark J. Ratain, *Combination Therapy Patents: A New Front in Evergreening*, 39 NATURE BIOTECH. 1504, 1504 (2021) (citation omitted); *see also* Traficonte & Armstrong, *supra* note 5, at 340 (stating that one of the PHOSITA's features is their "skill level . . . within their field, with education or training as the usual benchmark") (citations omitted).

96. Mylan Pharms. Inc. v. Merck Sharp & Dohme Corp., No. IPR2020-00040, 2021 WL 1833325 (P.T.A.B. May 7, 2021), at *5 (affirming that the PHOSITA can be "(i) a Ph.D. in chemistry, biochemistry, medical chemistry, pharmacy, pharmaceutics, or a related field, and at least two years of relevant experience in drug development including an understanding of salt selection in drug development; (ii) a master's degree in the same fields and at least five years of the same relevant experience; or (iii) a bachelor's degree in the same fields and at least seven years of the same relevant experience").

97. *See, e.g.*, Samsung Bioepis Co. Ltd v. Alexion Pharms., Inc., No. IPR2023-01070, 2023 WL 8797049 (P.T.A.B. Dec. 19, 2023), at *6 (affirming that a "POSA also would have knowledge of laboratory techniques and strategies used in immunology research"); Novartis Pharms. Corp. v. Accord Healthcare Inc., No. CV 18-1043-KAJ, 2020 WL 13837968 (D. Del. Aug. 10, 2020), *aff'd*, 21 F.4th 1362 (Fed. Cir. 2022), *opinion vacated on reh'g*, 38 F.4th 1013 (Fed. Cir. 2022), *and rev'd*, 38 F.4th 1013 (Fed. Cir. 2022) (defining the PHOSITA as "a multi-disciplinary research team that includes 1) a Ph.D. with expertise in the area of neurology and/or an M.D. having several years of clinical experience treating multiple sclerosis patients, and who would be knowledgeable about the multiple sclerosis literature, and 2) a pharmacologist with experience in drug development") (citations modified); Immunex Corp. v. Sanofi, No. CV 17-02613 SJO (PLAx), 2018 WL 6252460 (C.D. Cal. Aug. 24, 2018), at *5 (affirming that "a POSITA would have knowledge of the scientific literature, knowledge of laboratory techniques and strategies used in immunology research, less formal education if that person had several additional years of experience employed in academic or corporate laboratories, or may have worked as part of a multidisciplinary team").

98. *See* Sage Prods., LLC v. Stewart, 133 F.4th 1376, 1382–83 (Fed. Cir. 2025).

decision concerning medical treatment explicitly mentioned the requirement of providing an explanation or evidence before including disparate arts in the PHOSITA construct.[99] It should be noted that while the PHOSITA can be equipped with multidisciplinary skills, the level of these skills must be ordinary.

3. Estimating the Degree of Creativity Exercised by the PHOSITA

In *KSR Int'l Co. v. Teleflex Inc.*,[100] the Supreme Court found that the PHOSITA must be "a person of ordinary creativity, not an automaton."[101] Notwithstanding that, scholars argue that pre-*KSR* U.S. precedents already demonstrated a tendency to recognize an increasing level of creativity by construing the PHOSITA as a professional researcher rather than a mechanic or a designer.[102] Specifically, ordinary creativity indicates that the PHOSITA has "common sense" and can employ "creative steps."[103]

First, the PHOSITA can rely on their common sense to glean suggestions from the prior art that go beyond its primary purpose.[104] Herein, the claimed common sense must be supported by "some articulated reasoning with some rational underpinning."[105] Despite this requirement, Pedraza-Farina and Whalen point out the risk that *KSR* can still allow judges to exercise discretion in discerning what constitutes common sense.[106] This creates a higher risk of hindsight bias.

Additionally, the *KSR* Court stated that judges can consider the inferences and creative steps that the PHOSITA would employ.[107] This empowers the PHOSITA with some level of inferential capacity, permitting them to "work with known methods to obtain predictable results."[108] Similar to common sense, the level of this inferential capacity remains unclear.

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99. Biofrontera Inc. v. Sun Pharm. Indus., Inc., No. IPR2024-01312, 2025 WL 594858 (P.T.A.B. Feb. 24, 2025), at *4 (rejecting petitioner's proposition that the PHOSITA needs to have "both an engineering degree and a medical degree" because petitioner did not submit any particular explanation or evidence in support).

100. 550 U.S. 398 (2007).

101. *Id.* at 420–21.

102. *See* Jonathan J. Darrow, *The Neglected Dimension of Patent Law's PHOSITA Standard*, 23 HARV. J.L. & TECH. 227, 243–44 (2009).

103. *KSR*, 550 U.S. at 418, 421.

104. *Id.*

105. *Id.* at 418; *see also* Arendi S.A.R.L. v. Apple Inc., 832 F.3d 1355, 1363 (Fed. Cir. 2016) ("[W]e conclude that while 'common sense' can be invoked, even potentially to supply a limitation missing from the prior art, it must still be supported by evidence and a reasoned explanation.").

106. Pedraza-Farina & Whalen, *supra* note 71, at 256–57.

107. *KSR*, 550 U.S. at 418.

108. Amy L. Landers, *Ordinary Creativity in Patent Law: The Artist Within the Scientist*, 75 MO. L. REV. 1, 70 (2010).

The *KSR* decision was criticized for not providing further details on the creative process, leaving the above-mentioned terms prone to ambiguity and malleability.[109] On the lower limit of such creativity, some scholars believe the so-called "ordinary creativity" to starkly contrast with an automaton mindset — the mindset of someone who merely pieces together prior knowledge without engaging in any genuine thought.[110] On its upper limit, however, the boundary is still unclear.

### *B. AIDD Brings Tremendous Uncertainties to the Existing PHOSITA Paradigm*

Before *KSR*, some scholars credited the PHOSITA for providing flexibility for analysis in patent law, allowing it to accommodate new technologies.[111] While the doctrine arguably contributed to patent law's goal to spur innovation, its resilience has been facing challenges arising from the rise of interdisciplinary research and development.[112] Although increasingly sophisticated technologies have expedited drug discovery and development, these technologies did not drastically expand the capabilities of the PHOSITA. In light of *AliveCor, Inc. v. Apple Inc.*,[113] this Section argues that the advent of AIDD may finally change that. The development of AIDD can significantly reshape the knowledge, skill, and creativity of both the PHOSITA and real-world inventors and bring about tremendous uncertainties. Due to such uncertainties, the PHOSITA in the context of interdisciplinary pharmaceutical research may ultimately fail to accurately reflect inventive realities, demonstrating inventive capacities that are unreasonably disconnected from a real-world skilled artisan in the relevant art. Accordingly, this may render the threshold of non-obviousness unreasonably high or low, failing to identify truly meaningful innovations and exclude mediocre inventions from being patented. This has significant implications for NCE patents, which are widely cherished as the core of the incentive for new drug discovery and development.[114]

In accordance with the judicial practices outlined above,[115] this Section systematically examines the impact of AIDD on three foundational dimensions of the PHOSITA: (1) defining the pertinent art(s),

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109. *Id.* at 7, 70.

110. *See, e.g.*, Robin Feldman, *Artificial Intelligence and Cracks in the Foundation of Intellectual Property*, 76 UC L.J. 47, 82 (2024).

111. *See, e.g.*, Dan L. Burk & Mark A. Lemley, *Biotechnology's Uncertainty Principle*, 54 CASE W. RSRV. L. REV. 691, 692 (2004).

112. *See* Michal Shur-Ofry, *Connect the Dots: Patents and Interdisciplinarity*, 51 U. MICH. J.L. REFORM 55, 57 (2017).

113. 130 F.4th 1006 (Fed. Cir. 2025).

114. *See* S. Sean Tu, *The Long CON: An Empirical Analysis of Pharmaceutical Patent Thickets*, 86 U. PITT. L. REV. 213, 215 (2024).

115. *See supra* Section III.A.

(2) determining the level of ordinary skill, and (3) calibrating the scope of ordinary creativity.

1. Reconsidering the Pertinent Art(s): Knowledgeable PHOSITA or Ignorant PHOSITA in the Pharmaceutical Industry?

As discussed, an interdisciplinary PHOSITA is not impossible in U.S. patent law. If interdisciplinary collaboration was a norm in the field of the claimed invention by the relevant time, patent examiners and judges can account for prior art from previously disparate technical fields in the analysis of a single invention. In the field of health technologies, the Federal Circuit in *AliveCor* implicitly affirmed the Patent Trial and Appeal Board's finding that the PHOSITA "may be a member of an interdisciplinary team including persons with backgrounds in electrical engineering, mechanical engineering, biomedical engineering, computer science, and/or cardiology".[116] Therefore, in the context of AIDD, a PHOSITA in the pharmaceutical field can simultaneously have knowledge in computer science, insofar as knowledge in computer science is routinely utilized in the field by the relevant time. Also, as previously discussed, the PHOSITA is presumed to know all prior art references in these fields.[117] Accordingly, a PHOSITA in the age of AI will possess a continuously enlarging body of interdisciplinary knowledge. This may render the legal hypothetical extraordinarily knowledgeable, and consequently, more pharmaceutical inventions may appear obvious to them.

By contrast, some scholars downplay the effects of AI and view it as a tool for bridging the gap between the legal construct of the PHOSITA and an actual inventor. For example, Villasenor argues that AI is a powerful tool in helping the PHOSITA discover the prior art.[118] Nevertheless, this argument fails to recognize the dynamics within the pharmaceutical industry. Both training data and models are usually kept confidential. Pharmaceutical companies tend to maintain the confidentiality of data obtained from drug R&D[119] for its importance to foundational model tuning and arguably its value in assisting with specific molecule generation and optimization tasks. Industrial stakeholders have bemoaned that despite some disclosure of data and standardization efforts, the size of any consistently generated dataset for a specific task

116. Apple Inc. v. AliveCor, Inc., No. IPR2021-00972, 2022 WL 17463245 (P.T.A.B. 2022), at *9, *aff'd*, 130 F.4th 1006 (Fed. Cir. 2025).

117. *See supra* note 84 and accompanying text.

118. *See, e.g.*, John Villasenor, *Ten Thousand AI Systems Typing on Keyboards: Generative AI in Patent Applications and Preemptive Prior Art*, 26 VAND. J. ENT. & TECH. L. 375, 394 (2024).

119. *See* E. Richard Gold & Robert Cook-Deegan, *AI Drug Development's Data Problem*, 388 SCI. 131, 131 (2025).

is usually smaller than the proprietary datasets within large pharmaceutical institutions.[120]

The opacity of crucial datasets creates a dilemma. While current rules appear to broadly extend the PHOSITA's knowledge scope, it nevertheless cannot cover confidential information and eventually does not reflect the knowledge level of a real skilled artisan in the AIDD era.

2. Uncertain Level of Ordinary Skill: Omnipotent PHOSITA or Incapable PHOSITA?

With the expansion of the prior art, the level of ordinary skill may also rise. Remarkably, using AI models for drug discovery and development can be considered a laboratory technique and strategy employed in the pharmaceutical industry.[121] As the industry increasingly adopts AIDD models, it is reasonable to expect the PHOSITA to have access to these models and broadly deploy relevant techniques. In *AliveCor*, the Federal Circuit found that the PHOSITA could use machine learning "generally" in the way that the cited references taught and beyond its primary purposes.[122] Building on this conclusion, the PHOSITA in the pharmaceutical industry can arguably use any machine learning algorithm disclosed in the prior art, regardless of whether or not it was initially intended for a particular drug R&D field.

Prior to *AliveCor*, scholars and industrial stakeholders had expressed some valid concerns with equipping the PHOSITA with access to AI. From a technical standpoint, humans fundamentally do not have an AI's data-driven learning capability.[123] Accordingly, some pharmaceutical companies believe that a PHOSITA having access to AI is equivalent to a natural person possessing extraordinary rather than ordinary skills.[124] Additionally, some commentators question the technological sophistication and diffusion of AIDD. For example, Chun contends that AIDD is still at an early stage and far from rendering drug discovery a predictable field that drastically elevates the threshold of

120. Cas Wognum, Jeremy R. Ash, Matteo Aldeghi, Raquel Rodríguez-Pérez, Cheng Fang, Alan C. Cheng et al., *A Call for an Industry-Led Initiative to Critically Assess Machine Learning for Real-World Drug Discovery*, 6 NATURE MACH. INTELL. 1120, 1120 (2024).

121. *See supra* note 97 and accompanying text.

122. AliveCor, Inc. v. Apple Inc., 130 F.4th 1006, 1015 (Fed. Cir. 2025) (noting that the PHOSITA may apply the general machine learning teachings from prior art to the claimed invention and need not be limited to the precise uses disclosed in the references).

123. Tabrez Y. Ebrahim, *Data-Centric Technologies: Patent and Copyright Doctrinal Disruptions*, 43 NOVA L. REV. 287, 309 (2019).

124. *See, e.g.*, Amgen, Comment Letter on Request for Comments Regarding the Impact of the Proliferation of Artificial Intelligence on Prior Art, the Knowledge of a Person Having Ordinary Skill in the Art, and Determinations of Patentability Made in View of the Foregoing (July 30, 2024), at 22, https://downloads.regulations.gov/PTO-P-2023-0044-0054/attachment_1.pdf [https://perma.cc/9U5N-B7WX].

non-obviousness.[125] Similarly, the Pharmaceutical Research and Manufacturers of America alleges that the use of AIDD is a recent phenomenon and remains highly experimental.[126] Echoing this, Villasenor argues that adjusting the PHOSITA based on cutting-edge technologies with limited accessibility is misguided, as these advanced tools are often prohibitively expensive and available only to a small subset of inventors.[127] Finally, industrial stakeholders have mentioned that any effort to equip the PHOSITA with access to AI should take into account the fragmented deployment of AIDD models in different areas of technology.[128] With respect to NCEs, separate models for generation and optimization may be involved. Therefore, attempting to incorporate AI models into the PHOSITA analysis can be even more arduous if more than one model is involved.

Despite these concerns, the PHOSITA analysis should still account for the use of AI tools. The level of technological diffusion should not constitute a valid ground for fundamentally preventing AI from being a part of the PHOSITA analysis. Nor does the fact that a certain technique requires "extensive time, money, and effort to carry out" prevent it from being "arguably 'routine' to one of ordinary skill in the art."[129] Provided that AIDD will be prevalent in the foreseeable future, a rigorous examination of its influence on the PHOSITA is warranted. At the same time, precedents acknowledge that the PHOSITA may possess highly advanced tools that demonstrate extraordinary functions. The Federal Circuit confirmed in *Kubin* that the PHOSITA can have access to the well-known and reliable techniques in the prior art.[130] In fact, it even concluded that these advanced techniques can render previously "unpredictable" results in an advanced art "predictable".[131] The court departed from conventional assessments of the PHOSITA by attributing to them an enhanced capacity to reasonably predict successful outcomes in biotechnology — particularly cross-species genetic extrapolation.[132] Rather than clinging to previous acknowledgements of the inherent unpredictability and complexity embedded in isolating

125. Chun, *supra* note 31, at 32–33.

126. PhRMA, Comment Letter on Request for Comments Regarding the Impact of the Proliferation of Artificial Intelligence on Prior Art, the Knowledge of a Person Having Ordinary Skill in the Art, and Determinations of Patentability Made in View of the Foregoing (July 29, 2024), at 4–5, https://downloads.regulations.gov/PTO-P-2023-0044-0052/attachment_1.pdf [https://perma.cc/5587-29XX].

127. Villasenor, *supra* note 118, at 394.

128. PhRMA, *supra* note 126, at 5.

129. Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348, 1367 (Fed. Cir. 2007).

130. *In re* Kubin, 561 F.3d 1351, 1360 (Fed. Cir. 2009).

131. *Id.*

132. *Id.* (explaining that given "the well-known and reliable nature of cloning and sequencing techniques in the prior art," a skilled artisan would be able to clone the gene encoding a known protein, supporting the conclusion that cross-species genetic extrapolation — such as isolating a human gene based on analogous techniques and information from other species — falls within the ordinary capabilities of PHOSITA).

genetic sequences, the court assumed that routine methodological proficiency and clearly defined experimental pathways would enable the PHOSITA to anticipate results reliably.[133] Therefore, the *AliveCor* decision aligns with established case law.

From a normative perspective, disregarding AIDD in the PHOSITA analysis can exacerbate patent abuse. An empirical study found that exploiting continuation patents ("CONs") can expand the scope of claims and deter competitors from generic entry.[134] By using CONs to derive new claims from the specification of a primary patent that already covers an NCE, patent holders can obtain patents on minor variations of the original invention while claiming the same priority date.[135] Because AIDD significantly enhances the predictability of molecules, pharmaceutical institutions can facilitate the screening of the neighboring chemical space of existing patented NCEs and argue that their specifications can cover new variations that were initially not claimed by the prior patent. According to Shuang Liu, AIDD can mitigate some challenges of doing so, such as the requirements of enablement and written description.[136] Therefore, AIDD may inadvertently facilitate the above-mentioned malpractice by lowering technical barriers. This conflicts with the public health goals that distinguish pharmaceutical patents from other patents. The U.S. has introduced a series of legislations, such as the Hatch-Waxman Act,[137] to spur innovation as well as accelerate generic entry to enable broader access to affordable medications. The fundamental objective of patent law is to protect those truly meaningful innovations that "promote the [p]rogress of [s]cience and useful [a]rts."[138] In order to achieve these objectives, U.S. patent law should endeavor to ensure that AIDD technologies widen public access to affordable medicines rather than becoming a tool for excluding competition and impeding public health. To prevent this, the PHOSITA must by no means remain unaffected by AIDD.

A crucial question remains to be answered: To what extent can AIDD elevate the PHOSITA's skill level? Because the PHOSITA is

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133. *See id*.

134. *See* Michael A. Carrier & S. Sean Tu, *Why Pharmaceutical Patent Thickets Are Unique*, 32 TEX. INTELL. PROP. L.J. 79, 86 (2024) (explaining that continuation patents, though sharing the same expiration date as their parent, can be strategically filed in multiple generations to create dense patent thickets comprised of overlapping and sometimes questionable claims and that because each continuation must differ from the parent, patentees can tailor new claims to specifically target rival products as they enter the market); *id*. at 103–07 (presenting and discussing empirical findings).

135. Tu, *supra* note 114, at 217–21.

136. Shuang Liu, *A Helper for Patenting the "Unpredictable": Artificial Intelligence*, 23 MINN. J.L. SCI. & TECH. 671, 677 (2022) (explaining that AI-assisted drug discovery tools allow inventors to meet the enablement and written description requirements under U.S. patent law by enabling broader genus claims with reduced experimental burden).

137. Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act, Pub. L. No. 98–417, 98 Stat. 1585 (1984).

138. U.S. CONST., Art. I, § 8, cl. 8.

presumed to have access to all publicly available machine learning algorithms and model architectures, this assumption may raise questions about whether the PHOSITA can make fair and reliable determinations of the obviousness of an NCE, particularly if AIDD becomes a widely used tool in the pharmaceutical industry. In this scenario, both the performance of all publicly available AIDD models and the PHOSITA's skill of using these models should be examined and considered. This test faces several challenges. First, the disclosed state of prior art can be potentially lower than the level of an average model. Pharmaceutical institutions currently do not fully disclose the configurations of AIDD models and confidential datasets in publicly available documents. However, as mentioned, both model configurations and training datasets have significant impacts on model performance.[139] Second, even if all AI models are disclosed, it would still be arduous to determine the performance of the average AIDD model due to the lack of reproducibility and explainability of these models.[140] Lastly, precisely accounting for the influence of human-AI interactions is also difficult.

3. Ordinary Creativity: Rigid or Supreme Creativity?

AIDD also fuels the eternal uncertainties brought by the "ordinary creativity" standard. To what extent can AIDD boost the ordinary creativity of the PHOSITA? In *AliveCor*,[141] the Federal Circuit cited *KSR* and held that the PHOSITA can use known machine learning algorithms in ways different from their original purposes, make inferences, and employ creative steps.[142] Specifically, such creativity may include modifying existing algorithms and applying them with different types of data.[143] While this may not enable the PHOSITA to make dramatic changes to the configurations of models or select markedly different training datasets, it can still significantly alter the overall performance of AIDD models even with minor revisions.[144] Consequently, it is possible to see that an ordinarily creative PHOSITA may be capable of using models that significantly excel or underperform existing models. Eventually, the bar of non-obviousness may significantly rise or fall relative to the realities of the inventive process. All in all, the application of *KSR's* flexible "ordinary creativity" standard to AIDD may introduce even greater uncertainty, as it inherently considers minor modifications to intrinsically volatile AIDD models.

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139. *See supra* Section II.C.1.

140. Tim W. Dornis, *Artificial Intelligence and Innovation: The End of Patent Law as We Know It*, 23 YALE J.L. & TECH. 97, 129–30 (2020); *see supra* Section II.C.3.

141. 130 F.4th 1006 (Fed. Cir. 2025).

142. *Id.* at 1015.

143. *See id.*

144. *See* Aliper et al., *supra* note 55 and accompanying text.

In summary, AIDD will significantly disrupt the obviousness analysis by complicating the construction of the PHOSITA. While it is almost certain that the progression and diffusion of AIDD tools can strengthen the PHOSITA by expanding its already massive knowledge scope and amplifying prodigious creativity, accurately assessing its impacts remains analytically challenging. First, the fact that pharmaceutical institutions rarely disclose AIDD model configurations and training datasets can cause the PHOSITA's capabilities to be significantly lower than that of a real inventor equipped with AI. Second, even if all relevant information is publicly available for analysis, it is still technically difficult to determine the level of ordinary skill possessed by a PHOSITA having access to AI models due to reproducibility issues. Furthermore, in the post-*KSR* era, incorporating the dimension of ordinary creativity further complicates the analysis of the PHOSITA's capabilities, rendering the assessment increasingly intractable.

In existing literature, commentators are split on whether AI will make obviousness too demanding or too permissive. A number of scholars, such as Abbott and Chun, have expressed concerns that the adoption of AI tools might render innovations eventually obvious and not eligible for patent protection.[145] Leading patent attorneys, such as Tull and Miller, argue that the use of AIDD models may render inventions obvious "even where the 'finite number of identified, predictable solutions' is beyond that of human calculation."[146] In this scenario, the incentives of pharmaceutical institutions can be seriously undermined, and subsequent development such as clinical trials will likely be abandoned given the absence of patent protection.

However, the non-obviousness analysis can lead to the exact opposite result as well. Since the prior art in the analysis strictly excludes confidential datasets and model parameters held by pharmaceutical companies, the PHOSITA is necessarily modeled to have access to a substantially narrower informational base than actual innovators in the age of AIDD. This informational constraint does not operate in isolation. As a result, pharmaceutical inventions generated through industrial actors' AI systems may appear disproportionately "unexpected" and thus less obvious from the PHOSITA's perspective.[147] Crucially, this perceived unexpectedness does not reflect the intrinsic technological difficulty of the invention, but is rather an artifact of the asymmetry between the capabilities assumed for the PHOSITA and those deployed

145. *See, e.g.*, Abbott, *supra* note 91, at 2; Chun, *supra* note 31, at 33–34.

146. *See, e.g.*, Susan Y. Tull & Paula E. Miller, *Patenting Artificial Intelligence: Issues of Obviousness, Inventorship, and Patent Eligibility*, 1 RAIL 313, 320 (2018) (citation omitted).

147. *Cf.* Shlomit Yanisky-Ravid & Regina Jin, *Summoning a New Artificial Intelligence Patent Model: In the Age of Crisis*, 2021 MICH. ST. L. REV. 811, 835 (2021) (comparing AI inventions with non-AI inventions and arguing that the black-box nature of AI algorithms might make AI-generated outputs appear unexpected).

in practice. As a result, applicants may unreasonably acquire more patents at the expense of public interests.

If the legal hypothetical is to keep playing its central role in the non-obviousness analysis, a fair construction of the PHOSITA is mandatory to strike a balance between innovation incentive and public health. Then, can we expect judges and examiners to achieve this goal? The answer is likely to be negative. Within the opaque and data-driven landscape of AIDD, the inherently constrained scope of the PHOSITA's knowledge and the uncertainty and ambiguity surrounding their skill level and creativity create significant hurdles. Even for examiners, who generally possess more expertise in the relevant fields,[148] evaluation of model functionality remains an arduous task.[149]

## IV. A CRITICAL REVIEW OF EXISTING PROPOSALS

In response to the aforementioned challenges, several scholars, practitioners, and industrial stakeholders have put forward various proposals to accommodate these changes. This Part reviews a selection of proposals, which were primarily chosen for their practical feasibility.[150] Most selected proposals focus on the broader notion of AI-generated inventions, with only a limited subset specifically addressing pharmaceutical inventions. While the foregoing analysis points to significant uncertainties, current proposals are largely based on the assumption that AI-assisted inventions may be unpatentable for being obvious. Notwithstanding that, several of these proposals remain

148. PowerOasis, Inc. v. T-Mobile USA, Inc., 522 F.3d 1299, 1304 (Fed. Cir. 2008) (stating that examiners "are assumed to have some expertise in interpreting the references and to be familiar from their work with the level of skill in the art") (quoting Am. Hoist & Derrick v. Sowa & Sons, 725 F.2d 1350, 1359 (Fed. Cir. 1984)).

149. One of the reasons why patent examiners may face systematic constraints in evaluating AI model functionality is limited disclosure by applicants. *See* Mateo Aboy, Aparajita Lath, Timo Minssen & Kathleen Liddell, *The Sufficiency of Disclosure of AI Inventions*, 19 J. INTELL. PROP. L. & PRAC., 834, 840 (2024) (finding substantial insufficiency of disclosure in granted patents that claim medical artificial intelligence); Arti K. Rai, *The Reliability Response to Patent Law's AI Challenges*, 59 U.C. DAVIS L. REV. 97, 128 (2025) (finding that only a fairly small number of patents held by AI-native pharmaceutical companies mentioned the use of AI).

150. For an alternative proposal beyond the scope of this Article, see Raina Haque, Simone Rose & Nick DeSetto, *The Non-Obvious Razor & Generative AI*, 25 N.C. J.L. & TECH. 399, 440 (2024) (suggesting that the USPTO could "maintain proprietary GenAI models, perhaps indexed by month, year, or even day" to approximate the capabilities of contemporaneous industry systems, with examiners using these models as a proxy for what an ordinarily skilled artisan would have obtained by querying a commercially available GenAI system). Another proposal, while not directly focused on addressing how PHOSITA should be constructed in the age of AI, is closely relevant to solving the issue. *See* Tabrez Y. Ebrahim, *Artificial Intelligence Inventions & Patent Disclosure*, 125 PENN. ST. L. REV. 147, 211–14 (2020) (recommending that the USPTO incentivize the inventor's voluntary disclosure of AI use with prioritized examination and lower maintenance fees).

valuable for illuminating the structural deficiencies inherent in the PHOSITA-centric non-obviousness framework.

In light of the degree to which each proposal departs from the current framework, these proposals can be broadly categorized into three approaches: (1) the *status quo* approach, (2) the reformist approach and, (3) the replacement approach.

### *A. The Status Quo Approach*

Under the *status quo* approach, emerging AIDD technologies may not, at least in the foreseeable future, necessitate fundamental changes to the current legal framework. The existing analytical framework is often regarded as sufficiently adaptable and flexible given its evolutionary character. Within this perspective, scholarly attention has focused on determining the ordinary level of AI technology.

#### 1. The Ordinary AI Under the Current Approach

Some scholars believe the PHOSITA framework can naturally adapt in each of its three prongs. For example, Romm argues that "expanding the scope of prior art to include tools that a PHOSITA would have access to" and assuming that the PHOSITA will have "the good sense to use" them is enough.[151] In tandem, Schellekens suggests that humans can "enrich their knowledge" through interaction with AI models and "[a]s ever more sophisticated Al means enter the normal toolkit of the P[HO]SITA, the bar of inventiveness will rise automatically."[152] Despite the extensibility of the current framework, this proposal still cannot effectively address the uncertainties with analyzing the capabilities of a PHOSITA using AI models, particularly because it does not involve executable steps to reliably construct the PHOSITA in a way that accurately gauges its capabilities.

#### 2. The Ordinary AI Based on Mandatory Disclosure

To mitigate the uncertainties more effectively, Truong argues that the mandatory disclosure of AI use can help reflect the state of the art in AI technology.[153] Additionally, Truong refers to federal regulations and case law, positing that the USPTO is authorized to demand the disclosure of AI use, which is reasonably necessary for determining the

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151. *See* Connor Romm, *Putting the Person in PHOSITA: The Human's Obvious Role in the Artificial Intelligence Era*, 62 B.C. L. REV. 1413, 1445–46 (2021).

152. Maurice Schellekens, *Artificial Intelligence and the Re-Imagination of Inventive Step*, 13 J. INTELL. PROP. INFO. TECH. & ELEC. COM. L. 89, 97 (2022).

153. Kenny Truong, *Expanding Nonobviousness To Account for AI-Based Tools*, 104 J. PAT. & TRADEMARK OFF. SOC'Y 51, 66–67 (2024).

patentability of the claimed invention.[154] Nevertheless, the doctrinal reasoning of mandatory model disclosure is partially flawed. While the USPTO is authorized to demand the information key to the patentability of the claimed invention,[155] it seems to hold a cautious attitude towards actively exercising and enforcing it. According to a statement by the Director of the USPTO, the exercise of such authority only occurs in rare cases.[156] Crucially, if deemed material to patentability, the information related to the model will inevitably be disclosed to the public upon patent issuance,[157] which may evoke concerns regarding intrusion into corporate confidential information. Finally, even if all the models are accessible to the USPTO examiners, it would still be arduous to accurately determine the PHOSITA in practice.[158]

3. Deeming Uncreative AI as the Ordinary AI

In lieu of following the conventional steps for constructing the PHOSITA, some scholars advocate for characterizing the ordinary AI as an uncreative model that is already disclosed in the prior art.[159] While this approach initially prevents the threshold of inventiveness from becoming too high, presuming AI models to be uncreative may run afoul of the doctrine of ordinary creativity set forth in *KSR*. Although one may argue that ordinary creativity can be demonstrated by the human user of the AI model rather than the model itself, restricting the PHOSITA's toolkit can already constitute rigid restrictions on creativity. Practically speaking, as AIDD models inherently boost creativity, the proposal risks setting the bar unreasonably low for inventions directed toward AIDD. Additionally, publicly available AIDD models may be less advanced than the average AIDD model used confidentially by industrial stakeholders.

The *status quo* approach faces substantial and multifaceted challenges in practice. Whether through flexible reinterpretation of the PHOSITA, mandatory disclosure of AI use, or the characterization of AI as inherently uncreative, each measure fails to provide a consistent, administrable, and reality-reflective method for assessing inventive

154. *Id.* at 67–68; 37 C.F.R. § 1.105 (2024).

155. 37 C.F.R. § 1.105 (2024).

156. Kathi Vidal, *AI and Inventorship Guidance: Incentivizing Human Ingenuity and Investment in AI-Assisted Inventions*, U.S. PAT. & TRADEMARK OFF. (May 2, 2024), https://www.uspto.gov/blog/ai-and-inventorship-guidance-incentivizing [https://perma.cc/R6AK-QJS9] ("As AI becomes ubiquitous, including as people build on each other's AI-assisted inventions, it will become increasingly difficult to identify the ways in which AI plays a role in the inventive process. Therefore, the USPTO is not, at this time, implementing any new requirement to disclose the use of AI, beyond that which is required in rare circumstances by USPTO rules.").

157. MPEP § 724.04 (9th ed. Rev. 01.2024, Nov. 2024).

158. *See supra* Section III.B.

159. *See, e.g.*, Yanisky-Ravid & Jin, *supra* note 147, at 848.

capacity. Accordingly, regardless of the possibility of mandating AI disclosure, the current legal framework cannot reliably construct a PHOSITA that reflects the realities of the pharmaceutical inventive process in the age of AIDD.

### *B. The Reformist Approach*

While acknowledging the flaws of the existing framework, certain scholars propose amendments to the internal elements of the PHOSITA analysis to enhance its long-term viability in the era of AI. From a structural lens, the PHOSITA is composed of two interrelated elements: (1) a hypothetical human character, and (2) a field-specific skill threshold. Correspondingly, scholars have suggested reforms that target each prong.

#### 1. Revising the "Person" in PHOSITA

##### *a. Team Having Ordinary Skill in the Art*

Some scholars propose expanding the conventional notion of the "person" in PHOSITA to encompass a team. Traficonte and Armstrong, for instance, introduce the concept of the "Team Having Ordinary Skill in the Art[]" ("THOSITA"), which reconceptualizes the hypothetical person as a multidisciplinary team.[160] While their proposal is not specifically designed to address AIDD inventions, they note that THOSITA may incidentally offer analytical benefits in incorporating AI into a framework of collective human collaboration.[161] Furthermore, when AI's capabilities reach a certain level, a "THOSITA-plus" standard that equips a team with AI may be essential to reflecting the reality of heightened skills.[162]

However, the existing PHOSITA standard already allows for a person to be equipped with interdisciplinary knowledge and expertise. Therefore, the doctrinal distinction between a single PHOSITA and a THOSITA may in practice yield only marginal differences in the nonobviousness analysis. Also, the THOSITA framework may bring even more uncertainties because of communication difficulties between team members,[163] which can be hard to gauge.

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160. Traficonte & Armstrong, *supra* note 5, at 334–35.

161. *See id.* at 367–68.

162. *Id.*

163. Dennis Crouch, *Person(s) Skilled in the Art: Should the Now Established Model of Team-Based Inventing Impact the Obviousness Analysis?*, PATENTLY-O (May 18, 2011), https://patentlyo.com/patent/2011/05/persons-skilled-in-the-art-should-the-now-established-

*b. Machine Having Ordinary Skill in the Art*

Alternatively, some scholars have called for replacing "person" with "machine," proposing a framework of "Machine Having Ordinary Skill in the Art." For example, Abbott predicts that machines would gradually replace humankind's role across different stages of drug R&D and eventually evolve to be a "natural substitute" for humans.[164] Nevertheless, fully automated inventive machines are still distant from reality. It would be more advisable to address the human-centric PHOSITA first. There are also technical obstacles to determining the reference model and applicable datasets for testing.[165]

2. Revising the "Skill" Possessed by the PHOSITA

Some scholars believe that a flexible approach for evaluating skill can help accommodate AI. As skill can be broadly interpreted to encompass both direct human contributions and tool functionality, commentators have advocated for (1) construing the level of skill as epitomized at a certain phase where a human makes significant contributions or (2) deeming it to be non-ordinary. Such approaches demonstrate a strong deviation from the obscure and holistic approach in *AliveCor*.

*a. Person Having Ordinary Skill in the AI*

Some scholars advocate for shifting the focus to human contribution to the pre-inventive stage of model training. Looking into human-AI collaboration, Reinbold argues for reconceptualizing the PHOSITA as the PHOSIAI: "Person Having Ordinary Skill in AI."[166] Reinbold recommends a three-prong analysis, which focuses on: (1) whether a skilled artisan would select the same algorithm and data used by the patent applicant or holder as the starting point, (2) whether the prior art and training data would motivate the PHOSITA to modify the algorithm to invent the claimed invention, and (3) whether there exists a reasonable expectation of success for the PHOSITA to create the claimed invention with the algorithm.[167]

While the proposal emphasizes human contribution to the invention, it raises potential concerns from a doctrinal standpoint.

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model-of-team-based-inventing-impact-the-obviousness-analysis.html [https://perma.cc/MJ28-2YVK] ("As compared to a solo worker, teams often have an overall broader depth of knowledge, but are often plagued by communication difficulties.").

164. Abbott, *supra* note 91, at 30.

165. *See* Schellekens, *supra* note 152, at 94–96.

166. Patric M. Reinbold, *Taking Artificial Intelligence beyond the Turing Test*, 2020 WIS. L. REV. 873, 879 (2020).

167. *Id.* at 892.

Patentability should be based on the claimed invention itself, and not be "negated by the manner in which the invention was made."[168] The Supreme Court has dismissed the idea that a patentable invention must reveal a "flash of creative genius" and clarified that the frame of mind of the inventors is irrelevant to the non-obviousness analysis.[169] Some may borrow insights from *In re Hoeksema*[170] and suggest that U.S. patent examiners and judges accept the argument that the inventive step contained in the process of discovering or developing the NCE can enhance the inventive step of the NCE derived from the process.[171] According to *Hoeksema*, "if the prior art of record fails to disclose or render obvious a method for making a claimed compound . . . it may not be legally concluded that the compound itself is in the possession of the public [or obvious]."[172] However, even disregarding the factual difference between "making" and "discovering" a drug, this potential proposal is still subject to multiple challenges. Under this approach, the inventiveness of the NCE is largely contingent upon the inventiveness of the AIDD model. Again, it is technically arduous to fairly and accurately determine whether an AIDD model is more inventive than others.

In addition, even if the comparison between AIDD models becomes technically feasible in the future, this approach would inevitably require the disclosure of the specifics of the relevant models. Mandatory disclosure of AI models, as previously discussed, risks intruding into corporate confidential information and evoking backlash.[173] Alternatively, voluntary disclosure of model details is arguably a more complicated scenario. While existing empirical research identifies the prevalent unwillingness to disclose AI use among AI-native pharmaceutical companies,[174] there exists a theoretical possibility that pharmaceutical companies would be incentivized to disclose model details in exchange for the lucrative rewards of obtaining a drug patent. Nevertheless, some additional considerations arising from the emerging commercial dynamics of AIDD can curb disclosure. For example, even if the pharmaceutical companies that sponsor subsequent commercialization were willing to disclose model details for drug patent monopolies, model providers could block the initiative. Currently, more and more traditional pharmaceutical companies enter into R&D collaboration with AI drug discovery companies and rely on the models

168. 35 U.S.C. § 103 (2011).
169. Graham v. John Deere, Co. of Kan. City, 383 U.S. 1, 15 n.7 (1966) (citation omitted).
170. 399 F.2d 269, 274 (C.C.P.A. 1968).
171. *See id.* at 274.
172. *Id.*
173. *See supra* Section IV.A.2.
174. *See* Rai, *supra* note 149 and accompanying text.

developed by the latter.[175] The collaboration agreements usually contain confidentiality clauses that strictly forbid the disclosure of model specifics.[176] Therefore, even if applicants or patentees would like to trade model specifics for drug patents, model providers may obstruct them.

*b. Person Having the Best Available Model in the Art*

Instead of attempting to define ordinary skill, some scholars advocate for abandoning ordinariness. Gurgula, for example, invokes an English court ruling,[177] proposing the main solution as crediting a skilled artisan with the best available AI technology.[178] By doing so, this measure reframes the question as whether a skilled artisan equipped with the best available models instead of a technically average model, at the time of invention, would find the claimed invention obvious. This approach can overcome the practical difficulties of determining the ordinary AI model.

However, there are still doctrinal and technical challenges. Primarily, the proposal is devoid of jurisprudential foundation under U.S. patent law, whereby a PHOSITA is strictly supposed to possess ordinary skill as distinct from the best available technology. In *AliveCor*, the court did not delimit the skill of machine learning as being at the highest level.[179] Furthermore, given the rapidly increasing sophistication of AIDD models, it is burdensome to keep looking for the best available technology at the relevant time. As patent litigation only takes place after the patent application is filed, it is also difficult for examiners and judges to determine the best technology at a particular point in the past, especially if there have been radical breakthroughs since then. Accordingly, examiners and judges are arguably more likely to be subject to hindsight bias and underestimate the inventiveness of the claimed invention. Selecting "a single outstanding" AIDD model in the market as the best AIDD model would be infeasible, especially as the owner of

175. *See Pharmaceutical Partnerships with AI Drug Discovery*, GALEN GROWTH, https://www.galengrowth.com/product/pharmaceutical-partnerships-with-ai-drug-discovery [https://perma.cc/DZE5-KXSF] ("91 pharma giants formed 900+ partnerships; Pfizer, Bayer, and Eli Lilly at the forefront with 13 each.").

176. *See, e.g.*, Exscientia PLC, Amended and Restated Collaboration Agreement between Bayer AG and Exscientia Ltd. (Exhibit to Form F-1/A) 38 (Sep. 17, 2021), https://www.sec.gov/Archives/edgar/data/1865408/000110465921116988/tm2119783d9_ex10-9.htm [https://perma.cc/R9UP-EH4E] ("The Receiving Party will take all reasonable precautions, including adequate data safety measures, to maintain the confidentiality of the Disclosing Party's Confidential Information. . . .").

177. Genentech Inc.'s Patent (Human Growth Hormone), [1989] RPC 147, 278 (U.K.) ("[W]e should credit the hypothetical team with the best available equipment to see whether, so equipped, they could have found their way to a solution without exceeding the permitted maximum of inventive thinking.").

178. *See* Gurgula, *supra* note 31, at 14–15.

179. *See* AliveCor, Inc. v. Apple Inc., 130 F.4th 1006, 1015–16.

the model would be disadvantaged as their AI outputs would be found obvious.[180]

### *C. The Replacement Approach*

Apart from the foregoing PHOSITA-related approaches, other commentators have formulated alternative analytical frameworks distinct from the PHOSITA hypothetical framework. Depending on the temporal focus, these approaches can be categorized as pre-solution and post-solution strands.

#### 1. Pre-Solution Strand

Before being instructed to find technical solutions for a specific problem, AIDD models must undergo data training and model tuning, as well as receive a specific instruction. At this stage, human experts can contribute to the AIDD inventions by selecting data, validating models and optimizing algorithms, or putting forward the question for AIDD models to solve. Scholars recommend that the non-obviousness of AIDD inventions can be supported by a) establishing new secondary considerations, or b) the formulation of unknown questions.

##### *a. Secondary Considerations Based on the Pre-Solution Process*

Traditionally, secondary considerations, also known as objective evidence, have been relied upon to determinatively reverse the *prima facie* finding of obviousness in pharmaceutical patent cases.[181] Apart from judges, patent examiners are also obligated to consider secondary considerations during patent prosecution.[182] Unlike other factors under the Graham Framework, secondary considerations pay more attention to non-technical aspects such as economic and motivational issues and provide more convenience for judges to comprehend.[183] By anchoring the non-obviousness analysis in objective evidence, the assessment can also mitigate hindsight bias arising from the subjective PHOSITA analysis.[184] At the same time, secondary considerations are non-exhaustive

180. Dornis, *supra* note 140, at 133.

181. *See* Christopher M. Holman, *The Role of Objective Indicia in Assessing the Nonobviousness of Pharmaceutical Inventions*, 37 BIOTECH. L. REP. 4, 15 (2018); Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530, 1538 (Fed. Cir. 1983) ("[E]vidence of secondary considerations may often be the most probative and cogent evidence in the record. It may often establish that an invention appearing to have been obvious in light of the prior art was not.").

182. MPEP § 2141(II) (9th ed. Rev. 01.2024, Nov. 2024).

183. Graham v. John Deere, Co. of Kan. City, 383 U.S. 1, 35–36 ("These legal inferences or subsets do focus attention on economic and motivational rather than technical issues and are, therefore, more susceptible of judicial treatment than are the highly technical facts often present in patent litigation.").

184. Holman, *supra* note 181, at 5.

and constantly evolve. Lower courts have formulated new kinds of secondary considerations such as "disbelief of experts" and simultaneous development by competitors.[185]

Some scholars, therefore, believe that secondary considerations can still serve as reliable safeguards of non-obviousness in the age of AIDD and recommend introducing new secondary considerations based on evidence obtained from stages prior to invention. For example, Haque, Rose, and DeSetto advocate for the consideration of the degree of specialization and proprietization of training data, as well as a model's capacity to "perform a specific function, solve a specific problem, or reason about a specific field" relative to other more ubiquitous models.[186] Furthermore, Reinbold predicts that courts and the USPTO may use new factors such as "the relative minimum and maximum amount of data selected by the user, the ability of the user to preliminarily narrow and select the range of usable data, the labeled or unlabeled nature of the data, the user's motives, and the specific prior uses of each form of machine learning and algorithms."[187] Admittedly, these proposals constitute a deviation from a model's specific operations by instead comparing the model, data, and training process independently. This effectively circumvents the complexities inherent in establishing causal relationships between human contributions and the final output.

Nevertheless, courts now tend to rigidly analyze the nexus between the specific limitations of the claimed invention and the cited objective evidence.[188] This requirement aims to ensure that the evidence genuinely pertains to the invention's technical merits, rather than to other factors extraneous to patentability. The foregoing proposed evidence (such as the degree of data specialization, proprietization, or selection) arguably faces substantial challenges in establishing such nexus. They are largely related to the preparation of the essential materials for the inventive process rather than the final invention. Such upstream factors do not reproducibly or deterministically yield the particular claim limitations, therefore struggling to establish the requisite nexus between the asserted evidence and the invention's technical merits. Additionally, it is still technically arduous to compare the performance of

185. *Id.* at 6 & 6 n.13.

186. Haque et al., *supra* note 150, at 443.

187. Reinbold, *supra* note 166, at 902–03.

188. *See, e.g.*, Fox Factory, Inc. v. SRAM, LLC, 944 F.3d 1366, 1373 (Fed. Cir. 2019) ("[P]resuming nexus is appropriate when the patentee shows that the asserted objective evidence is tied to a specific product and that product embodies the claimed features, and is coextensive with them.") (citations omitted); Purdue Pharma L.P. v. Accord Healthcare, Inc., No. 2023-1953, 2024 WL 5244764, at *10 (Fed. Cir. Dec. 30, 2024), *cert. denied*, 146 S. Ct. 95 (2025); Janssen Pharms., Inc. v. Teva Pharms. USA, Inc., 97 F.4th 915, 933 (Fed. Cir. 2024); Application of Dill, 604 F.2d 1356, 1361 (C.C.P.A. 1979) ("The evidence presented to rebut a prima facie case of obviousness must be commensurate in scope with the claims to which it pertains.").

different models. Furthermore, the proposal may implicitly discourage competition because crediting the specialization and proprietization of training data in patentability analysis risks granting further competitive advantages to brand pharmaceutical companies, which are more likely to possess valuable databases. Simultaneously, industrial stakeholders may be incentivized to withhold the sharing of relevant data, narrowing other stakeholders' access to valuable information. As a result, the proposal may increase the likelihood of market failure.

*b. Formulation of Unknown Problems*

Alternatively, another group of scholars advocate for reframing the non-obviousness analysis into a "problem-solution" dual structure, with an emphasis on the identification of the problem rather than the inventive process of the solution. This framework erodes the role of the PHOSITA, as the primary focus is on whether the problem identified by the inventor was previously unknown. Hao cites *In re Omeprazole*,[189] proposing that the non-obviousness analysis should shift focus to a "problem finder" (i.e., a natural person involved in R&D) in lieu of a "problem solver" (i.e., an AI system).[190] In sum, Hao suggests that identifying a specific problem can by itself demonstrate inventiveness.

Notwithstanding that, the technical burden of identifying an unknown problem can be eased by advanced AI tools, which can detect hidden patterns and relationships.[191] Previously inconspicuous problems may become easier to detect with the use of AIDD tools. From a doctrinal perspective, the proposal is subject to more challenges. First, the Federal Circuit has ruled against the persuasiveness of the identification of an unknown problem argument if an independent motivation irrelevant to the identified problem can motivate the PHOSITA to combine prior art.[192] As AIDD also extends the breadth and depth of the PHOSITA's thinking, it can enable them to find such independent motivations without touching upon the unknown problem. Second, the

189. 490 F. Supp. 2d 381, 534 (S.D.N.Y. 2007), *aff'd*, 281 F. App'x 974 (Fed. Cir. 2008), *and aff'd on other grounds*, 536 F.3d 1361 (Fed. Cir. 2007) (noting that identifying the causes of the problems and solving them in the manner disclosed in the challenged patents would not be obvious to a PHOSITA).

190. Yuan Hao, *The Rise of "Centaur" Inventors: How Patent Law Should Adapt to the Challenge to Inventorship Doctrine by Human-AI Inventing Synergies*, 104 J. PAT. & TRADEMARK OFF. SOC'Y 71, 106 (2024).

191. *See supra* Section II.C.2.

192. Janssen Pharms., Inc. v. Teva Pharms. USA, Inc., 97 F.4th 915, 929 (Fed. Cir. 2024) ("[A]lthough identifying a recognized problem or need in the prior art is one way to demonstrate motivation . . . the motivation analysis is not limited by the problem or need recognized by the inventors."); ImmunoGen, Inc. v. Stewart, 130 F.4th 1328, 1333 (Fed. Cir. 2025) (noting that the specific problem addressed by the inventors being previously unknown "does not necessarily mean that the dosing regimen itself was not obvious," and thus rejecting the argument that identifying and solving an unknown problem alone establishes non-obviousness).

interpretation of what constitutes an "unknown" problem is also flexible. While precedents did not explicitly interpret an "unknown" problem as non-obvious to the PHOSITA, the non-obviousness argument is undermined if the same solution has been used to solve a similar problem.[193] This implies a stricter stance regarding what constitutes an "unknown" problem in the non-obviousness analysis. In fact, if a problem is obvious to identify for the PHOSITA, it would be arguably more difficult for patent applicants or owners to prove non-obviousness with this approach.

2. Post-Solution Strand

Some commentators also explore the possibilities of reconsidering the inventive step by examining the evidence generated after the formulation of a technical solution. In this sphere, commentators have discussed both conventional secondary considerations and reproducibility.

*a. Conventional Secondary Considerations: The Lifeline?*

As noted previously, conventional secondary considerations have played a pivotal role in rebutting *prima facie* findings of obviousness in pharmaceutical patent cases.[194] However, only some of these secondary considerations can play a potentially significant role in the AIDD scenario. When the rejection decision happens at the patent prosecution stage, a common and frequently adopted secondary consideration, namely, commercial success, may not even be considered as it can only be assessed after FDA approval, which is usually granted years after applicants obtain the patent.[195] This Section will only discuss the ex ante secondary considerations that are available for analysis during patent prosecution.[196]

i. Long-Felt but Unsolved Need and Failure of Others

If an art-recognized problem existed for a long time without solution, the claimed invention that solves such problem is more likely to overcome obviousness.[197] It is principally "analyzed as of the date of

193. Application of Wiseman, 596 F.2d 1019, 1023 (C.C.P.A. 1979).

194. *See* Holman, *supra* note 181, at 4.

195. Rebecca S. Eisenberg, *Pharma's Nonobvious Problem*, 12 LEWIS & CLARK L. REV. 375, 383 (2008) ("[T]he most common form — commercial success — may only be observed ex post.").

196. *See supra* notes 148–49 and accompanying text. Erroneous patent decisions are already likely to arise during the prosecution stage. This Article seeks to underscore addressing relevant underlying issues at that phase.

197. *See* MPEP § 716.04(I) (9th ed. Rev. 01.2024, Nov. 2024) ("Establishing long-felt need requires objective evidence that an art recognized problem existed in the art for a long period of time without solution.").

an articulated identified problem and evidence of efforts to solve that problem."[198] Nevertheless, if a similar product treating the same disease has already appeared before the claimed invention and even received approval from the FDA,[199] or if the time frame of the need is short,[200] or if the need is narrowly construed by judges,[201] the existence of such product can undermine the persuasiveness of the aforementioned argument. Judges have noted that the long-felt need inquiry is usually coupled with the failure of others inquiry, and a proper combination of the two arguments can be significantly probative of non-obviousness.[202] Regarding the failure of others inquiry, if other competitors fail to invent products that tackle the relevant problem, it could help negate a reasonable expectation of success.[203]

For these reasons, Fabris believes that the long-felt but unsolved need factor can play a significantly more active role in defending the inventiveness of AIDD.[204] This factor is generally highly persuasive in pharmaceutical invention cases because the jury, which plays a substantial role in determining factual issues, tends to identify health as a prime necessity and acknowledges related "long felt need[s]."[205] Additionally, the long-felt but unsolved need factor can circumvent the challenges arising from AIDD models' lack of explainability.[206] One may

198. Tex. Instruments Inc. v. Int'l Trade Comm'n, 988 F.2d 1165, 1178 (Fed. Cir. 1993).

199. Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc., 752 F.3d 967, 978 (Fed. Cir. 2014) (finding that the persuasiveness of evidence of unexpected results or non-obviousness was weakened where a similar compound for the same indication had already been invented and even FDA-approved before the claimed invention and stating that a mere difference in degree, rather than kind, is insufficient to rebut obviousness).

200. *See, e.g.*, Adapt Pharma Operations Ltd. v. Teva Pharms. USA, Inc., 25 F.4th 1354, 1376 (Fed. Cir. 2024) (finding that "[the] need, even if unmet, was not so long felt that it overcomes the strong case of obviousness, particularly in view of the plethora of prior art references" where the purported need was urgent and began three years before the patent's priority date).

201. Amerigen Pharms. Ltd. v. Janssen Oncology, Inc., No. IPR2016–00286, 2018 WL 454509, at *16 (P.T.A.B. Jan 17, 2018) (noting that while the invention could nearly always satisfy a long-felt need if it contributes to increasing cancer patient survival rates, sufficient evidence should be presented to prove that a specific long-felt need existed for the method of administering abiraterone acetate and prednisone).

202. Adapt Pharma Operations Ltd., 25 F.4th at 1376; Millennium Pharms., Inc. v. Sandoz Inc., 862 F.3d 1356, 1369 (Fed. Cir. 2017) ("Evidence of long-felt need is 'particularly probative of obviousness when it demonstrates both that a demand existed for the patented invention, and that others tried but failed to satisfy that demand.'") (citation omitted).

203. *In re* Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig., 676 F.3d 1063, 1081 (Fed. Cir. 2012) ("Evidence that others tried but failed to develop a claimed invention may carry significant weight in an obviousness inquiry. . . . This is particularly true when the evidence indicates that others found development of the claimed invention difficult and failed to achieve any success.") (citations omitted).

204. *See* Daniele Fabris, *From the PHOSITA to the MOSITA: Will "Secondary Considerations" Save Pharmaceutical Patents from Artificial Intelligence?*, 51 IIC-INT'L REV. INTELL. PROP. & COMPETITION L. 685, 701 (2020).

205. *See id.* at 702.

206. *Id.* at 703.

also argue that this factor can be coupled with the failure of others to further enhance persuasiveness.

However, the proposal is doctrinally flawed. AIDD can effectively erode the persuasiveness of long-felt but unmet need. On the one hand, AIDD raises the threshold for secondary considerations to reverse obviousness by leading to a stronger showing of a *prima facie* finding of obviousness. This is because secondary considerations should be strong enough to overcome a *prima facie* finding of obviousness.[207] On the other hand, AIDD can directly weaken long-felt need and failure of others arguments. With marvelous capabilities, AIDD may facilitate competitors' simultaneous R&D progress, effectively reducing the likelihood for long-felt need to arise. Simultaneous inventions that are independently developed by other competitors may undermine the probative value of long-felt but unmet need as evidence of non-obviousness, particularly where an exogenous development — such as advancements in artificial intelligence — enables multiple parties to readily achieve results that previously remained unattainable.[208] By a similar rationale, judges can adjust their analyses of the failure of others inquiry, considering competitors to be "equipped with the same knowledge, the same equipment, and the same assistance of AI machine learning."[209] Consequently, this factor may also be less effective.

ii. Unexpected Results

If the claimed invention demonstrates improved properties much greater than what would have been predicted, it is more likely for an invention to be non-obvious.[210] Empirical research suggests that the majority of the early post-*KSR* cases in which patent holders successfully reversed an obviousness finding involved the submission of

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207. *See, e.g.*, ZUP, LLC v. Nash Mfg., Inc., 896 F.3d 1365, 1375 (Fed. Cir. 2019) ("The weak evidence of secondary considerations presented here cannot overcome the strong showing of obviousness."). The Federal Circuit also mentioned that it was rare to find that evidence of secondary considerations outweighed a strong *prima facie* case of obviousness. *See* Transocean Offshore Deepwater Drilling, Inc. v. Maersk Drilling USA, Inc., 699 F.3d 1340, 1354 (Fed. Cir. 2012) ("Few cases present such extensive objective evidence of nonobviousness, and thus we have rarely held that objective evidence is sufficient to overcome a prima facie case of obviousness.").

208. Brendan Bargmann & Robert A. Bohrer, *Alphafold 3, AI, Antibody Patents, the Future of Broad Pharmaceutical Patent Claims and Drug Development*, 53 AIPLA Q.J. 247, 275 (2025) ("Mark Lemley has suggested that 'simultaneous invention can defeat long-felt need where some exogenous shock (like AI here) means that everyone could easily achieve what they had long been unable to do.'") (citation omitted).

209. Reinbold, *supra* note 166, at 902.

210. Procter & Gamble Co. v. Teva Pharms. USA, Inc., 566 F.3d 989, 997–98 (Fed. Cir. 2009) (crediting expert testimony and experimental evidence demonstrating that the claimed compound exhibited unexpectedly high potency and a markedly improved toxicity profile relative to the cited prior art); Leo Pharm. Prods., Ltd. v. Rea, 726 F.3d 1346, 1358 (Fed. Cir. 2013) (noting that the presentation of extensive experimental evidence of unexpected results contradicted obviousness finding).

evidence of "unexpected results."[211] This factor could help preserve non-obviousness in the age of AIDD.[212]

Nevertheless, this factor's effectiveness also depends on its "weight against evidence supporting *prima facie* obviousness."[213] In recent years, there has been a trend to raise the bar of effectiveness of unexpected results. The Federal Circuit in *Vanda* ruled that the claimed invention was obvious because there was a reasonable expectation of success based on prior art.[214] As of now, it remains unclear whether the Supreme Court's decision acknowledges the reasonable-expectation-of-success test as the rule for determining the inventive step of pharmaceutical inventions. The Federal Circuit has provided some clues. Where evidence of unexpected results is presented, to be "particularly probative," it must still demonstrate the difference between the claimed invention and its closest prior art and that such difference would not have been expected by a PHOSITA at the relevant time.[215] Scholars have also argued for stricter limitations on this factor. Notably, Lemley argues that if a claimed invention is already obvious to try in the first place, no matter how astonishing the result is, it should be regarded as lacking an inventive step.[216] Therefore, the feasibility of this factor may also face more hurdles.

*b. Reproducibility: Can the Claimed Inventions Be Re-Generated?*

Since the subjective construct of the PHOSITA is extremely burdensome in the AI era, some scholars believe that reproducibility can be adopted as another form of objective evidence. For example, Abbott recommends assessing the ability of "the machine selected to represent

211. Natalie A. Thomas, *Secondary Considerations in Nonobviousness Analysis: The Use of Objective Indicia following KSR v. Teleflex*, 86 N.Y.U. L. REV. 2070, 2089 (2011) ("Overall, the majority of patent cases where secondary considerations were found to support a finding of nonobviousness involved . . . a particular type of evidence traditionally categorized as secondary (unexpected results).").

212. *See* Rose Hughes, *Insilico Medicine: Lessons in IP Strategy from a Front-Runner in AI-Drug Discovery*, IPKAT (Feb. 4, 2025), https://ipkitten.blogspot.com/2025/02/insilico-medicine-lessons-in-ip.html [https://perma.cc/FAY8-BX3E].

213. MPEP § 716.02(c) (9th ed. Rev. 01.2024, Nov. 2024); *see supra* note 207 and accompanying text.

214. Vanda Pharms., Inc. v. Teva Pharms. USA, Inc., 2023-1247, No. 2023-1247, 2023 WL 3335538, at *4–5 (Fed. Cir. 2023), *cert. denied*, 144 S.Ct. 1393 (2024) (explaining that because the prior art provided a skilled artisan with a reasonable expectation of success in achieving the claimed result, the evidence of unexpected results was insufficiently persuasive to overcome the strong showing of obviousness).

215. Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc., 752 F.3d 967, 977 (Fed. Cir. 2014).

216. Mark A. Lemley, *Expecting the Unexpected*, 92 NOTRE DAME L. REV. 1369, 1370 (2017) (arguing that when unexpected results and reasonable expectation of success conflict, the latter should prevail because if ordinary scientists are already motivated and correctly expect to succeed, achieving the result reflects normal scientific progress rather than inventive insight).

the standard" to independently reproduce the claimed invention.[217] If the standard machine can reproduce the invention without undue experimentation, then the claimed invention is more likely to be obvious. Since it emphasizes the permissible number of attempts, the rationale of the proposed doctrine is akin to one of the rationales for proving obviousness, namely, the "obvious-to-try" doctrine, which provides that an invention is obvious if the PHOSITA can identify a finite number of known and predictable solutions and has a reasonable expectation of success in pursuing them.[218]

However, the proposal is not free from criticisms. Firstly, as acknowledged, reproducibility could be largely dependent on the training data.[219] Compared to real-world inventors, the PHOSITA can only consider publicly available data for the reproducibility test. While Abbott also argues that reliance on proprietary data may decrease "as machines become highly advanced,"[220] this may not happen in the pharmaceutical industry, which requires various multi-modal datasets spanning multiple stages. Lastly, determining the permissible number of experimentations is difficult.

The foregoing analysis suggests that all existing proposals face considerable hurdles either for being unable to accurately reflect the level of ordinary skill and creativity of the PHOSITA, or for wrongfully focusing on the particular manner of arriving at the invention, rather than the claimed scope of invention. This highlights a sequence of analytical complexities involved in determining the knowledge and skill of the PHOSITA within the context of AIDD. First, it is both doctrinally and practically challenging to glean substantial information pertinent to AIDD models and human-AI interaction in a collaborative environment. Even if the USPTO obtains profound access to such information, significant challenges persist with accurately constructing the ordinary skill of the PHOSITA based on the information. Beyond that, the more unpredictable and arduous challenge of precisely defining and evaluating "ordinary creativity" remains unresolved. Therefore, the complexities inherent in these analytical dimensions collectively underscore that the very nature of the PHOSITA appears increasingly incompatible with the technical features of AIDD. All these factors, coupled with the norms of high confidentiality and unique regulatory dynamics characteristic of the pharmaceutical industry, leave tremendous uncertainties to the construct of the PHOSITA. Accordingly, the objective evidence cannot effectively restore clarity as it used to. As NCE patents simultaneously incentivize pharmaceutical innovation and strongly impact public health, it is necessary to reformulate alternative

217. *See* Abbott, *supra* note 91, at 42.
218. MPEP § 2143(I)(E) (9th ed. Rev. 01.2024, Nov. 2024).
219. *See* Abbott, *supra* note 91, at 43.
220. *Id.*

proposals to diminish the uncertainties related to the PHOSITA and non-obviousness.

## V. RECOMMENDATIONS

Based on the foregoing problem identification and critique of existing proposals, this Part will discuss other feasible expedient measures for mitigating the influence of uncertainties in examining the non-obviousness of AIDD inventions under the existing legal framework. Beyond these expedient measures, it will further propose an alternative framework designed to offer a more sustainable and structurally robust solution for addressing these challenges over the long term.

This alternative framework proposes a new pathway, namely, the inventive commercial viability of the claimed invention, to displace the previous PHOSITA-centric obviousness analysis when AIDD tools become prevalent and extremely advanced in the pharmaceutical industry. To realize this, extensive cooperation and collaboration between the USPTO and the FDA is essential.

### *A. Other Feasible Strategies Under the Current Legal Framework*

Despite the PHOSITA's overarching influence in non-obviousness analysis, current rules still proffer several opportunities for making non-obviousness assessments based on a comprehensive and holistic evaluation of the claimed invention. This Section discusses how certain strategies may prove effective in the age of AIDD, at least temporarily.

#### 1. New Target: Discovering the Source of a Problem

An NCE designed and optimized by AIDD models can potentially demonstrate non-obviousness if it uncovers a new target for a disease. The inventive step may reside in the identification of the underlying cause of a pathological condition, even if the corresponding therapeutic solution would be considered obvious once the source of the problem is revealed.[221] As biological targets are integral components of the cause of a disease, an NCE that exerts its therapeutic effect by binding

221. *In re* Sponnoble, 405 F.2d 578, 585 (C.C.P.A. 1969) ("It should not be necessary for this court to point out that a patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified.").

to a novel biological target, commonly referred to as first-in-class drug, may significantly strengthen its claim to inventiveness.[222]

From the perspective of public interest, it is arguably fair and reasonable to patent first-in-class drugs. Irrespective of any unreasonable limitations attributed to the knowledge base of a PHOSITA, NCEs that unveil novel biological targets hold significant therapeutic promise. Patent protection is essential for recognizing their contributions to scientific breakthroughs and incentivizing subsequent commercialization that benefits public health. At the same time, when analyzing the obviousness of such inventions, examiners and judges are also less likely to find that a PHOSITA would have been able to combine or modify the prior art to arrive at the claimed inventions with a reasonable expectation of success. One may argue that the PHOSITA can predict new targets and tailor molecules that bind to them with the aid of AIDD models. Nonetheless, this requires substantial evidence to prove the PHOSITA can effortlessly determine new targets and develop the novel molecules that rely on them with publicly accessible AIDD models. This takes more effort than merely finding a molecule itself obvious.

2. New Property: Unexpected Progress in Other Properties

An NCE derived by AIDD models may also establish its value if it achieves significant progress in other properties apart from efficacy. An invention is more likely to demonstrate "unexpected results" if it produces "a new property dissimilar to the known property" rather than "a predictable result but to an unexpected extent" in efficacy.[223] For example, evidence of unexpected non-addictiveness of a drug can enhance its non-obviousness even though the improvements on efficacy were expected.[224]

The comprehensive evaluation of an NCE includes efficacy, safety, addictiveness, and selectivity. An NCE that demonstrates efficacy and progress in other properties deserves patent protection for its potential of facilitating public health. Also, current AIDD models are still far from accomplishing comprehensive multi-parameter optimization due to limitations in techniques, data scarcity, ethical concerns, and other

222. *See* Michael Lanthier, Kathleen L. Miller, Clark Nardinelli & Janet Woodcock, *An Improved Approach to Measuring Drug Innovation Finds Steady Rates of First-In-Class Pharmaceuticals, 1987–2011*, 32 HEALTH AFFS. 1433, 1434–35 (2013) ("Although subsequent approvals within the same class may prove to have advantages over the first drug, first-in-class drugs are genuinely innovative, because each represents a novel approach to drug therapy.").

223. UCB, Inc. v. Actavis Labs UT, Inc., 65 F.4th 679, 693 (Fed. Cir. 2023) ("A difference of degree is not as persuasive as a difference in kind — i.e., if the range produces 'a new property dissimilar to the known property,' rather than producing a predictable result but to an unexpected extent.") (citation omitted).

224. *See In re* May, 574 F.2d 1082, 1093 (C.C.P.A. 1978).

relevant factors.[225] This arguably still leaves sufficient room for reducing the chance of finding obviousness. Finally, with scientific and technological progress, the evaluation methodology for drugs may also continue to evolve. Novel desired properties of pharmaceuticals are likely to emerge over time. The European Medicines Agency, for example, has explicitly proclaimed its goal to comprehensively assess the value of new endpoints.[226] This evolving framework for assessing drug quality supports the continued use of unexpected improvements in alternative properties to demonstrate non-obviousness, particularly as AIDD models advance their multi-parameter optimization capabilities. Therefore, unexpected improvements on different properties can still constitute justifications for granting NCE patents in the era of AIDD.

In brief, some unique strategies under the current legal framework can still demonstrate certain amount of evidentiary value for establishing non-obviousness by simultaneously manifesting public benefits and overcoming technological hurdles. With these strategies, at least the highly innovative NCEs can secure patent protection and incentivize subsequent clinical research for commercialization. However, these strategies are mainly for tackling the underlying issue of an unreasonably high threshold for non-obviousness. Even in this regard, these strategies may not be a long-term solution, as AIDD models will continue to evolve and develop increasingly advanced and sophisticated capabilities. Consequently, the marginalized PHOSITA may come back and raise the same challenges against non-obviousness. To enable patent law to comprehensively protect all meaningful pharmaceutical inventions, secure certainties, and facilitate public health, structural reform is essential.

### *B. A Shift from Non-Obviousness to Inventive Commercial Viability*

While the preceding Section examined interim strategies that operate within the existing non-obviousness framework, these measures

225. *See* Rachel DeVay Jacobson, *The AI Drug Revolution Needs a Revolution*, 2 NPJ DRUG DISCOVERY 10, 1–2 (explaining that current AIDD approaches in multi-parameter optimization remain limited because most efforts focus on "optimizing molecules without improving our understanding of human biology and physiological responses to potential therapeutics"); Kang Zhang, Xin Yang, Yifei Wang, Yunfang Yu, Niu Huang, Gen Li et al., *Artificial Intelligence in Drug Development*, 31 NATURE MED. 45, 52 (2025) (noting that current AIDD models continue to face substantial challenges in multi-parameter optimization, as existing research tends to focus on optimizing chemical space while neglecting other key objectives such as druggability and synthesizability); Amir Elalouf, Hadas Elalouf, Ariel Rosenfeld, Hanan Maoz, *Artificial Intelligence in Drug Resistance Management*, 15 3 BIOTECH. 126, 17 (2025) (noting that the scarcity of reliable data and ethical concerns are main obstacles to AIDD's application in addressing drug resistance).

226. EUROPEAN MEDICINES AGENCY, *EMA Regulatory Science to 2025: Strategic Reflection, EMA 21 (2020),* https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection_en.pdf [https://perma.cc/78BM-S5L6].

remain constrained by the non-obviousness doctrine which is increasingly detached from the realities of pharmaceutical innovation. As such tools are unlikely to provide a sustainable solution, this Section advances a more fundamental shift. It calls for a conceptual reorientation of the patentability analysis by replacing non-obviousness with a new standard: inventive commercial viability. It is designed to align the patent doctrine with the dual imperatives of innovation and public health.

This Section first articulates a normative framework delineating the core attributes that an optimal patentability standard should encompass. It proceeds to introduce a novel alternative to the traditional non-obviousness requirement, namely, the standard of inventive commercial viability. The discussion then addresses anticipated procedural objections, before concluding with a critical assessment of the proposal's inherent limitations.

1. From Non-Obviousness to Inventive Commercial Viability: A Normative Reassessment

As discussed, the non-obviousness requirement heavily relies on the PHOSITA. Both primary and secondary considerations need to corroborate that the claimed invention is not obvious to the PHOSITA. Due to this dogmatic essence, non-obviousness may distract examiners and judges away from the fundamental purpose of NCE patents: encouraging meaningful pharmaceutical innovation and facilitating public health.

To further complicate the matter, the advent of AIDD brings enormous disruptions to the non-obviousness analysis of NCEs by rendering the PHOSITA uncertain. This may evoke public health concerns by either allowing inventors to obtain monopolies with patent mass-filings or disincentivizing inventors from conducting subsequent research on NCEs of varying degrees of innovativeness and commercializing these meaningful innovations.

The foregoing core objectives of NCE patents are informative. NCE patents are intended to afford sufficient incentives for pharmaceutical institutions to conduct subsequent R&D to pursue potential therapies.[227] The subsequent development, particularly clinical trials, is essential for gaining marketing approval, which allows medicinal products to be provided to the public and contribute to health. To commit tremendous funds and efforts to undertaking clinical trials, pharmaceutical institutions understandably attach considerable importance to the commercial viability of the candidate NCE. Therefore, the commercial viability of the claimed invention is essential for the applicant's

227. *See In re* Brana, 51 F.3d 1560, 1568 (Fed. Cir. 1995) (noting pharmaceutical patents help incentivize potential cures in areas like cancer through research and development before the grant of FDA approval).

economic motivation to pursue patent protection. If an NCE lacks the potential to pass regulatory review and enter the market as a treatment, the patent will fail to induce subsequent R&D investments. Therefore, an NCE that demonstrates insufficient commercial viability should not be protected by a patent. On top of that, inventions should be inventive. Patent law should protect meaningful innovations, rather than any minor technological improvements. Allowing such inventions to receive patent protection may narrow public access to affordable medicines and discourage pharmaceutical institutions from pursuing truly meaningful innovations.

The obviousness analysis arguably protects commercial viability to some extent and aligns with patent law's fundamental objective of protecting the truly meaningful inventions. By demanding that an invention should contain an inventive step, Section 103 can deter competitors from developing NCEs that are highly similar to prior art and ensure that pharmaceutical institutions have a safe zone for recouping investment in R&D.[228] Nevertheless, as discussed,[229] the framing of Section 103 points to a rigid application of the non-obviousness standard, drifting away from the core objectives of NCE patents.

To rectify this structural misalignment and better align patent doctrine with the goals of promoting health innovation and access, the current non-obviousness requirement should be replaced by a new patentability standard that centers on the objective inventiveness and commercial viability of the claimed invention, namely, inventive commercial viability. Under this proposed standard, inventive commercial viability refers to the integration of both technical inventiveness and commercial viability, which is epitomized by success in passing early-stage regulatory review. First, it is evident that patent protection should not extend to inventions that are merely commercially viable without demonstrating substantive innovation. On top of that, inventions that are technically inventive but fail to meet basic regulatory thresholds and enter the market should also fall outside the scope of patentability, as they cannot meaningfully contribute to public health and risk becoming exclusionary tools with limited societal value.

### 2. Implementing Inventive Commercial Viability: USPTO Authority, FDA Judgment

To implement the inventive commercial viability standard, this Section proposes a *sui generis* mechanism that links drug patent examination with regulatory review. Building upon preexisting initiatives,

228. *See* Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 TEX. L. REV. 503, 508 (2009) ("The patent system is an attempt to preserve the incentive to invest in R&D that would otherwise be vulnerable to free riding. . . .").

229. *See supra* Section IV.C.

the FDA would initiate an accelerated pathway for AIDD innovations, conditioned on the applicant's disclosure of key information regarding models, data, and training processes. The FDA would then assess the invention's efficacy, safety, and other relevant metrics during the review of IND application and share selected findings with the USPTO, which would retain independent authority to evaluate inventive commercial viability based on this input.

*a. Institutional Roles: USPTO as Decision-Maker, FDA as Technical Assessor*

Pursuant to the existing legal framework, the USPTO should still be the final decision-maker on the patentability of the claimed invention. In parallel, the FDA should be the technical assessor of inventive commercial viability. As the leading agency for pharmaceutical regulation, the FDA has plentiful expertise in examining new drugs. While it has long held authority over the commercial viability of drugs through IND application review, it also has the potential to be the ideal examiner of the inventiveness of pharmaceuticals.

First, pharmaceutical institutions are subject to asymmetric incentives regarding information disclosures to the FDA and the USPTO, favoring minimal disclosure to the USPTO, yet maximizing information provided to the FDA.[230] Since the FDA demands abundant evidence for approving clinical trials, pharmaceutical institutions tend to submit significant amount of data to fulfill the requirements.[231] Additionally, the FDA owes stringent confidentiality obligations regarding the information in IND applications,[232] which arguably covers

230. Garreth W. McCrudden, *Drugs, Deception, and Disclosure*, 38 BERKELEY TECH. L.J. 1131, 1139 (2023) ("The innovator is at once incentivized to share information about analogous competitor products with the FDA and to hide (or at least reframe) that same information when seeking patent exclusivity at the USPTO — even if the innovator suspects that the information speaks to the novelty or nonobviousness of their invention."); *see, e.g.*, Belcher Pharms., LLC v. Hospira, Inc., 11 F.4th 1345 (Fed. Cir. 2021).

231. *See, e.g.*, Mercidita Navarro, Nancy Brucken, Aiming Yang & Greg Ball, *Just Say No to Data Listings!*, 22 PHARM. STATS. 581, 581 (2023) (noting that "[s]ponsor companies often create voluminous static listings for Clinical Study Reports . . . and regulatory submissions . . . likely due to the perception that they are required and/or lack of knowledge of various alternatives").

232. *See* 21 U.S.C. § 331(j) (prohibiting "[t]he us[e] by any person to his own advantage, or revealing, other than to the Secretary or officers or employees of the Department, or to the courts when relevant in any judicial proceeding under this chapter, any information acquired under authority of . . . this title concerning any method or process which as a trade secret is entitled to protection"); 21 C.F.R. § 20.61(a) ("A trade secret may consist of any commercially valuable plan, formula, process, or device that is used for the making, preparing, compounding, or processing of trade commodities and that can be said to be the end product of either innovation or substantial effort. There must be a direct relationship between the trade secret and the productive process."); 21 C.F.R. § 20.61(b) ("Commercial or financial information that is privileged or confidential means valuable data or information which is used in

information related to the use of AI. Safeguarded by this, applicants are expected to disclose additional information to the FDA to demonstrate that their invention is truly AIDD-driven and to gain expedited approval for further research.

Second, the FDA has long administered various expedited review programs, such as Fast Track, Breakthrough Therapy, Accelerated Approval and Priority Review,[233] to support the development of drugs addressing unmet needs. These initiatives, along with the center-specific initiatives that also directly or indirectly facilitate the FDA review process,[234] demonstrate not only the agency's policy commitment to encouraging innovation, but also its institutional familiarity with balancing speed, safety, and scientific credibility. Over time, these programs have also fostered sustained channels of communication between the FDA and pharmaceutical institutions, allowing both sides to coordinate more effectively.[235] This accumulated experience enhances not only the efficiency of regulatory oversight, but also the strategic planning of R&D within the industry. In contrast, the USPTO lacks comparable experience in structuring or managing innovation-incentivizing pathways in the pharmaceutical context.

Finally, the FDA has greater capacity to evaluate pharmaceutical inventions. As noted, the FDA is widely recognized as the primary

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one's business and is of a type customarily held in strict confidence or regarded as privileged and not disclosed to any member of the public by the person to whom it belongs.").

233. *See Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Review*, U.S. FOOD & DRUG ADMIN. (June 12, 2023), https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review [https://perma.cc/23KA-64MD] (outlining currently available programs for speeding up drug regulatory process).

234. *See, e.g.*, *Oncology Center of Excellence*, U.S. FOOD & DRUG ADMIN. (Dec. 11, 2025), https://www.fda.gov/about-fda/fda-organization/oncology-center-excellence [https://perma.cc/3SFB-DGRT] (listing special programs for accelerating the review process for oncology drug development, including Real-Time Oncology Review ("RTOR"), Project Orbis, and Assessment Aid ("AAid")); *see also Model-Informed Drug Development Paired Meeting Program*, U.S. FOOD & DRUG ADMIN. (Jan. 15, 2026), https://www.fda.gov/drugs/development-resources/model-informed-drug-development-paired-meeting-program [https://perma.cc/8LB5-EYSH]; *CDER Initiatives*, U.S. FOOD & DRUG ADMIN. (Jul. 3, 2024), https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cder-initiatives [https://perma.cc/3FEY-YVBP] (listing the initiatives of the Center for Drug Evaluation and Research ("CDER") that aim to boost the efficiency of the drug development process, including 21st Century Review Initiative and Critical Path Initiative).

235. Alissa K. Wong, Maryam Mooghali, Reshma Ramachandran, Joseph S. Ross & Joshua D. Wallach, *Use of Expedited Regulatory Programs and Clinical Development Times for FDA-Approved Novel Therapeutics*, JAMA NETWORK OPEN, Aug. 31, 2023, at 1, 1 ("Fast track and breakthrough provide opportunities for increased interaction between manufacturers and the FDA."); Marquerita Algorri, Ajay Acharya, James Bernstein, Nina S. Cauchon, Xiao Hong Chen, Kim Huynh-Ba et al., *Meeting Report: Advancing Accelerated Regulatory Review with Real-Time Oncology Review (RTOR), Project Orbis, and the Product Quality Assessment Aid*, AAPS OPEN, Dec. 5, 2022, at 1, 8 ("Collectively, these initiatives enable direct and proactive communication between sponsors and regulators, as well as across global regulators.").

expert agency in matters of pharmaceutical regulation. This is rooted in its technical competence. In recent years, the FDA has significantly expanded its evaluative capacity by adopting novel assessment methodologies to enable more robust, data-driven oversight of pharmaceutical innovation.

For example, the FDA has increasingly embraced New Approach Methodologies ("NAMs") as part of its broader effort to modernize regulatory science. Notably, the FDA Modernization Act 2.0 explicitly authorizes the use of non-animal alternatives, such as *in vitro* cell-based assays and computational models, in regulatory submissions.[236] The FDA has endeavored to incorporate modelling and simulation for regulatory decision-making.[237] These consistent efforts have enabled the FDA to accrue growing confidence in the reliability and regulatory relevance of AI-generated simulation data. In April 2025, the FDA reaffirmed this trajectory by announcing plans to replace animal testing for monoclonal antibodies and other drugs with AI-based computational models and other advanced alternatives.[238] These developments collectively reflect the FDA's enhanced capacity to quantitatively evaluate pharmaceutical quality through data-driven and model-informed methodologies.

In addition, the FDA has initiated a proactive and collaborative regulatory program specifically tailored to AIDD. The agency has tentatively promoted a voluntary risk-based credibility assessment framework for the use of AI in drug development ("Draft Guidance").[239] According to the Draft Guidance, drug developers are encouraged to disclose model and development and evaluation processes to the FDA, covering descriptions of the model, developmental data (both training and tuning data), centralization of developmental data, model training techniques, and a review of model performance.[240] While the Draft Guidance is not legally binding, it outlines a potential

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236. 21 U.S.C. § 355 (2011), *amended by* 21 U.S.C. § 355(z) (2023) (defining nonclinical tests as "test[s] conducted in vitro, in silico, or in chemico, or a non-human in vivo test . . . [which] may include animal tests . . . cell-based assays, microphysiological systems, or bioprinted or computer models").

237. *See* Mason Marks, *Automating FDA Regulation*, 71 DUKE L.J. 1207, 1221–23 (2022).

238. *FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodies and Other Drugs*, U.S. FOOD & DRUG ADMIN. 2–3 (Apr. 10, 2025), https://www.fda.gov/news-events/press-announcements/fda-announces-plan-phase-out-animal-testing-requirement-monoclonal-antibodies-and-other-drugs [https://perma.cc/GS5F-EATP].

239. *See Considerations for the Use of Artificial Intelligence*, U.S. FOOD & DRUG ADMIN. (Jan. 6, 2025), https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-use-artificial-intelligence-support-regulatory-decision-making-drug-and-biological [https://perma.cc/8G43-HHDT] [hereinafter "Draft Guidance"].

240. *Id.* at 10–15.

FDA-endorsed framework for regulating AIDD models, one that emphasizes both transparency and voluntary compliance.[241]

By contrast, the USPTO lacks the resources and the scientific expertise necessary to perform comparable evaluations of pharmaceutical innovation. Unpredictable arts such as pharmaceutical inventions generally require high-level expertise and insights. This burden has been exacerbated by the surging number of patent applications involving multiple technologies.[242] Empirical studies suggest that examiners often grant invalid patents in the pharmaceutical industry due to a shortage of resources or applicants' complex strategies,[243] and the wrongful granting of patents further fortifies patent thickets and narrows market entry.[244] In light of this, the FDA's involvement is necessary for helping the USPTO overcome the foregoing institutional constraints.

*b. Specific Steps for Implementation*

First, the FDA should launch a separate fast-track initiative for pharmaceutical inventions developed through AIDD. Companies that rely on AIDD as a core discovery and development tool would be encouraged to proactively disclose key technical information to the agency, including model architecture, training data, and training process. Upon receiving these submissions, the FDA could employ NAMs and other advanced assessment methodologies to expeditiously evaluate the invention's safety, efficacy, and other related metrics. This process would enable the agency to form an informed, science-based understanding of the invention's overall quality prior to IND review. In particular, mechanisms such as pre-IND meetings can be relied upon for identifying and prioritizing drug candidates that demonstrate strong scientific promise,[245] thereby facilitating a more accelerated preclinical review process for highly innovative AIDD inventions. Notably, the Draft Guidance currently does not cover the drug discovery stage.[246] To further accelerate pharmaceutical development, future initiatives should explicitly incorporate the early-stage discovery process within the scope of regulatory engagement. Through this initiative, the FDA

241. *See* Sarfaraz K. Niazi, *A Critical Review of the FDA's Draft Guidance on Artificial Intelligence in Drug and Biological Product Regulation*, J. CHEMISTRY, Feb. 2, 2026, at 1, 14.

242. *See Intellectual Property: Patent Office Should Strengthen Its Efforts To Address Persistent Examination and Quality Challenges*, U.S. GOV'T ACCOUNTABILITY OFF. 14 (2025), https://www.gao.gov/assets/gao-25-107218.pdf [https://perma.cc/SK49-4ARJ].

243. Mark A. Lemley & Lisa Larrimore Ouellette, *Fixing Double Patenting*, 74 AM. U. L. REV. 1013, 1030 (2025) ("Scrutinizing the growing volume of continuing applications and other forms of double patenting is placing an increasing burden on the USPTO.").

244. *Id.* ("[W]hen under-resourced examiners make inevitable mistakes, 'patent thickets' can increase the cost of challenging or designing around patents.").

245. *See* Draft Guidance, *supra* note 239, at 17–20.

246. *Id.* at 3.

would also be positioned to assess the inventiveness of the NCE by benchmarking it against comparable compounds within its regulatory database.

Second, the FDA should conduct a systematic review of the IND application submitted for the AIDD-derived invention, drawing on the previously disclosed model and development information. While the fast-track mechanism facilitates early-stage engagement, the agency must maintain its scientific rigor and institutional credibility in evaluating the invention's safety and efficacy. This review can proceed within the existing regulatory framework for IND applications, which must be completed within 30 days of submission.[247] A positive IND determination not only authorizes the initiation of clinical trials, but also offers a regulatory indication of the invention's commercial viability.

Finally, the USPTO would independently determine the inventive commercial viability of the AIDD invention based on the information conveyed by the FDA. While successful IND clearance may indicate sufficient commercial viability, the question of inventiveness remains. Even if the claimed invention demonstrates extraordinary commercial viability, it would still fail the "inventive commercial viability" standard without a showing of sufficient inventiveness. Depending on the strength and clarity of the FDA's evaluation, the agency could either treat such recognition as sufficient to support a finding of inventiveness or, alternatively, develop its own evaluative benchmarks grounded in the FDA's methodological framework.

3. Defense

Given the novel and unconventional nature of the proposed pathway, concerns may arise regarding its potential doctrinal inconsistencies, particularly with respect to procedural aspects. This Section responds to such concerns with concrete evidence collected from legal practices and ongoing legislative initiatives.

By introducing a cooperative mechanism between the USPTO and the FDA, the proposal implicates a significant procedural shift. One may raise concerns with the risk of breaching confidentiality obligations in transmitting information from the FDA to the USPTO. The FDA is legally required to safeguard all submitted data as confidential, while the USPTO is under a duty to disclose any information material to patentability, even if initially submitted as confidential information, unless the patent application is abandoned and a petition to expunge is

247. 21 C.F.R. § 312.40(b) ("An IND goes into effect: (1) Thirty days after FDA receives the IND, unless FDA notifies the sponsor that the investigations described in the IND are subject to a clinical hold under § 312.42; or (2) On earlier notification by FDA that the clinical investigations in the IND may begin.").

filed.[248] The proposal can be tantamount to a *de facto* leak of FDA confidential data.

However, such concerns are likely overstated. From cross-agency data transmission to the publication of patent applications, current rules and industrial reactions offer a robust foundation for limited information sharing and publication. Primarily, the FDA is authorized to share certain confidential and other non-public information with other federal agencies.[249] Previously, the agency has reached Memoranda of Understanding with other federal agencies to share some confidential information to facilitate public health.[250] As this initiative also intends to further the interest of public health, it is principally legitimate for the FDA to share confidential information with the USPTO.

As regards the USPTO's publication of certain information, industrial stakeholders may not object to the disclosure of certain data contained in IND applications. Studies find that applicants may leverage Rule 132 as a tool to submit post-filing experimental data as evidence of "unexpected results" to overcome rejection based on non-obviousness.[251] Despite the eventual disclosure of confidential information, applicants are still willing to disclose such information in order to secure patents. Additionally, industrial stakeholders may welcome the use of FDA information at patent prosecution stage for its positive impacts on reducing litigation-related expenditures.[252] If eventually serious concerns with information disclosure still persist, it is also advisable to consider legislative reform and provide exemptions for the USPTO's obligation to publish confidential information material to patentability. For example, a bipartisan legislative proposal has been formulated to

248. MPEP § 724.04 (9th ed. Rev. 01.2024, Nov. 2024).

249. 21 C.F.R. § 20.85 ("[T]rade secrets and confidential commercial or financial information prohibited from disclosure . . . may be released only as provided by [the relevant] sections. Any disclosure under this section shall be pursuant to a written agreement that the record shall not be further disclosed by the other department or agency except with the written permission of FDA.").

250. *See MOU 225-24-023 with EPA/Office of Pesticide Programs, CDC, and USDA*, U.S. FOOD & DRUG ADMIN. (October 9, 2024), https://www.fda.gov/about-fda/domestic-mous/mou-225-24-023 [https://perma.cc/28TN-4FNW].

251. Tom Brody, *Declarations Under Rule 132 as a Tool for Rebutting Rejections for Obviousness, Anticipation, Nonenablement, or Lack of Written Description (Part One of Two)*, 102 J. PAT. & TRADEMARK OFF. SOC'Y 112, 113 (December 2021) ("Regarding the goal of overcoming § 103-rejections . . . [d]eclarations find use in submitting data from experiments that compare the claimed invention with the device, composition, or method that is disclosed by one of the cited prior art references. Here, the goal of the Declaration is to submit afterarising data demonstrating that the invention, as defined by the claims, can be distinguished from the device, composition, or method of the prior art.").

252. S. Sean Tu, *FDA Reexamination: Increased Communication between the FDA and USPTO to Improve Patent Quality*, 60 HOUS. L. REV. 403, 448 (2022) (explaining that the use of FDA information at the patent prosecution stage can reduce costly litigation and resource expenditures by helping to prevent the issuance of invalid patents, particularly in fields where patents are highly valuable and face a higher risk of inequitable conduct challenges, thus avoiding the need for later invalidity suits).

boost interagency information disclosure between the FDA and the USPTO to enhance communication and coordination in implementing activities related to pharmaceutical patents.[253]

4. Limitations

Despite the preceding defense, this proposal is still subject to inherent limitations. Notably, it does not seek to fully unlock the transformative potential of AIDD technologies. Rather than offering a comprehensive framework for spurring innovation, it is intended for functioning as an expedient mechanism within the patent law framework to mitigate doctrinal concerns surrounding non-obviousness. While it aims to promote fair and efficient examination of AIDD-related inventions, its primary focus remains on patentability, not on fostering systemic innovation or public health. As discussed, AIDD is fundamentally data-driven,[254] yet pharmaceutical institutions often retain relevant data as trade secrets, creating significant barriers to realizing its potential. Although this proposal does not directly address the structural deficit in data-sharing, it does make incremental progress by incentivizing unilateral disclosures to federal agencies, potentially steering regulatory the paradigm toward more innovation-conducive policies.

## VI. CONCLUSION

The rise of AIDD has introduced significant uncertainties into the doctrinal construction of PHOSITA, by disrupting its three components: delineating the pertinent art(s), assessing the level of ordinary skill, and calibrating ordinary creativity. These challenges have direct and far-reaching implications for evaluating the non-obviousness of NCEs. Existing reform proposals struggle to resolve the structural opacity surrounding the PHOSITA's role. Rather than continuing to anchor to the PHOSITA-centric non-obviousness analysis, it is more productive to revisit the core objectives of NCE patents — protecting truly inventive innovations that can be further developed for commercialization and facilitating public health. On this basis, attention should be directed toward the invention's technical inventiveness and its commercial viability. Ultimately, the task is to craft a patentability framework that proactively accommodates advanced technologies such as AIDD. Building on this foundation, the law must continue to strike a careful balance between incentivizing innovation and safeguarding

253. Interagency Patent Coordination and Improvement Act of 2025, S. 1097, 119th Cong. (2025). Notably, the Bill was previously introduced as S. 79 in the 118th Congress.

254. *See* Sadybekov & Katritch, *supra* note 2 and accompanying text.

public health. Although this paper focuses on pharmaceutical inventions, the analytical approach it proposes may offer broader relevance for assessing AI-generated inventions across technological domains.