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AI-assisted inventions in the field of drug discovery: readjusting the Inventive Step analysis

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ABSTRACT

Artificial intelligence ('AI') is increasingly applied at all stages of drug discovery. While AI has the potential to boost innovation, it also raises many important ethical, social, political, and legal issues. Among the latter are the challenges that AI poses for the patent system. With the rapid evolution of AI technologies and the increase in their computational power, the process of inventing has undergone substantial changes. As AI significantly expands human capabilities, inventions that were previously the result of human ingenuity, perseverance or serendipity can now be achieved by routine experimentations with the use of AI.

This article argues, therefore, that the patent law approaches that were developed to assess human-generated inventions are not suitable for AI-assisted inventions and requires urgent reconsideration. It will explain that the proper test for the obviousness assessment needs to take into account the advancement of AI technology and will provide suggestions on how the analysis can be modified.

Keywords: artificial intelligence, inventive step, obviousness, patents, drug discovery, access to medicines.

Introduction

The speed with which medical science has been developing over the past several decades is truly astonishing. It has brought many new techniques that allow researchers to enhance the process of drug discovery, such as next-generation sequencing, CRISPR technology, and high-throughput screening. Moreover, recent sequencing of the human genome has opened up the possibility of a more precise personalized medicine, which will allow healthcare professionals to tailor diagnosis and treatment based on the information from a patient's genome.[1] However, despite the progress in understanding biological systems and significant advances in technology, drug discovery remains a long, complicated, and inefficient process, which requires large investments and bears considerable commercial risks.[2] According to widely-cited industry figures, the process of developing a single drug, from the moment of selecting a compound until marketing, takes, on average, 10-15 years[3], with costs rising to as much as $2,6 billion.[4]

The pivotal problem is that the drug discovery process is fraught with uncertainty.[5] One of the most difficult stages in this process is finding and selecting new molecules for successful drugs.[6] This is because of the vast scale of potential pharmacologically active molecules, which may be as large as 10^{60} compounds; this is more small molecules than there are atoms in the Solar System.[7] Typically, it takes on average 4.5 years to discover and optimize candidates for preclinical testing,[8] for which thousands of compounds are often synthesized to find a promising lead compound.[9] Moreover, even when such a lead compound is identified, it may fail at a later stage. It is claimed that about 62% of new chemical entities in Phase IIb and Phase III clinical trials do not reach

[1] Carrasco-Ramiro, F., Peiro-Pastor, R. and Aquado, B. (2017). Human genomics projects and precision medicine. Gene Therapy, 24, 551–561; Viola, R. (2019). Finding the cures for cancer: AI and supercomputers paving the way to personalised medicine. Available at < https://ec.europa.eu/digital-single-market/en/blogposts/finding-cures-cancer-ai-and-supercomputers-paving-way-personalised-medicine>'.

[2] UNCTAD (2015). The role of competition in the pharmaceutical sector and its benefits for consumers. TD/RBP/CONF.8/3, 3.

[3] ibid.

[4] DiMasi, J.A. et al (2016). Innovation in the pharmaceutical industry: New estimates of R&D costs. Journal of Health Economics, 47, 26.

[5] Wolff, M.E. (2011). Drug discovery market exclusivity after KSR: The challenge to pharmaceutical scientists and the US congress. Journal of Pharmaceutical Sciences, 100(8), 3047.

[6] Workman P., Antolin A.A. & Al-Lazikani B. (2019). Transforming cancer drug discovery with Big Data and AI. Drug Discovery, 14:11, 1091.

[7] Mullard A. (2017). The drugmaker's guide to the galaxy. Nature, 549, 445–447.

[8] Paul, S. M. et al. (2010). How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nature Rev. Drug Discov. 9, 203–214.

[9] EFPIA (2018). The Pharmaceutical Industry in Figures. Key Data 2018, 2. Available at <https://efpia.eu/media/361960/efpia-pharmafigures2018_v07-hq.pdf>.

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the clinic.[10] The reason for such failures in late clinical stages is typically due to clinical safety and efficacy, followed by formulation, pharmacokinetics, bioavailability, and toxicity.[11] Furthermore, 80% to 90% of drug candidates are not approved by the U.S. Food and Drug Administration, typically due to lack of efficacy and safety, and poor dosage and endpoint selection.[12] Similar statistics have been observed in the EU.[13]

As a result of this complex, expensive, and uncertain process of drug discovery, the biopharmaceutical industry is under considerable pressure to expedite the development of new drugs, while reducing the cost of these activities.[14] 'Big data' may hold the key to the enhancement of this process. Such data comes from numerous sources, e.g., pre-clinical and clinical trials, clinic, labels of approved therapies, adverse event reports kept in drug safety databases, scientific papers, patents,[15] , etc. Combining various sets of data may help to unlock the understanding of the origins and processes of many diseases,[16] and, thus, can be invaluable for drug discovery. However, the sheer size, diversity, sparsity, and lack of structure of biological data make it extremely difficult for researchers to utilize and apply it effectively.[17] Moreover, it is constantly increasing in size. For instance, 'gene sequencing, which helps to identify gene mutations that cause diseases, generates terabytes of data' alone.[18] As a result, valuable knowledge that may help to unlock the secrets of diseases and speed up the process of drug discovery remains hidden behind these unexplored masses of information.

New emerging technologies may help to boost the process of drug discovery, making it more effective, speedy, and, most importantly, more predictable. With the advance of computational power, artificial intelligence ('AI') is increasingly employed in the biopharmaceutical field,[19] as it is becoming more efficient in sorting data, finding patterns and making predictions.[20] AI is a general term that covers several techniques and, in its widest meaning, can be described as a machine 'intelligence' that can mimic human behavior.[21] It includes a subfield called machine learning (ML), which uses statistical methods that enable computers to learn and make predictions without being explicitly programmed.[22] A further subfield of ML is deep learning (DL) that uses artificial neural networks, an approach to training algorithms inspired by the way our brains process information,[23] to learn from the vast amount of diverse data and improve its ability without task-specific programming.[24]

These sophisticated AI systems are increasingly applied at all stages of drug discovery and development.[25] Today, AI technologies can help with target identification,[26] the selection and optimization of lead compounds, and prediction of their effectiveness and side effects.[27] AI is also used to predict feasible synthetic routes for drug-like molecules,[28] pharmacological properties,[29] protein characteristics and efficacy,[30] drug combination and drug–target association.[31] Another promising field is drug repurposing, where AI is used to predict new molecular targets for known drugs.[32] These various applications of AI technology may provide an opportunity to counter the inefficiencies and uncertainties that arise in the traditional drug discovery process, minimizing bias and human intervention.[33]

While AI has the potential to boost innovation, it also raises several important ethical, social, political, and legal issues. Among the latter are the challenges that AI poses for the patent system. With the rapid evolution of AI technologies and the increase in their computational power, the process of inventing has undergone substantial changes. AI technologies have now reached such a level that they are capable of producing outputs with only limited human involvement. The application of AI in drug discovery is a good example of how

[10] Mak K.K & Pichika M.R. (2019). Artificial intelligence in drug development: present status and future prospects. Drug Discovery Today, 24(3), 775.
[11] ibid.
[12] Chen Y. et al. (2016). IBM Watson: How Cognitive Computing Can Be Applied to Big Data Challenges in Life Sciences Research, Clinical Therapeutics, 38, 688; Ismail K. & John L. (2004). Can the Pharmaceutical Industry Reduce Attrition Rates? Nat Rev Drug Discov, 3:711, 715; Sacks LV., et al. (2014). Scientific and Regulatory Reasons for Delay and Denial of FDA Approval of Initial Applications for new Drugs 2000-2012. JAMA, 378–384.
[13] Kashoki M. et al. (2020). A Comparison of EMA and FDA Decisions for New Drug Marketing Applications 2014–2016: Concordance, Discordance, and Why. Clinical Pharmacology & Therapeutics, 107: 1; Tafuri G. et al, (2013). Disclosure of grounds of European withdrawn and refused applications: a step forward on regulatory transparency. Br J Clin Pharmacol, 75(4), 1149–1151.
[14] Challener C.A., (2018). Can Artificial Intelligence Take the Next Step for Drug Repositioning? Pharmaceutical Technology Europe, 14 (discussing the application of an AI platform, Project Prodigy, which was developed by Biovista, that 'have led to repositioned drugs with animal model/cell line validation and issued or granted patents in multiple sclerosis, epilepsy, anti-glomerular basement membrane disease, and some rare diseases such as Friedreich's ataxia and Leber's hereditary optic neuropathy').
[15] Chen Y. et al. (2016). IBM Watson: How Cognitive Computing Can Be Applied to Big Data Challenges in Life Sciences Research, Clinical Therapeutics, 38, 695.
[16] Riccardo B. (2014). Big Data and Biomedical Informatics: A Challenging Opportunity. IMIA Yearbook of Med Inf., 8–13.
[17] Workman P., Antolin A.A. & Al-Lazikani B. (2019). Transforming cancer drug discovery with Big Data and AI. Drug Discovery, 14:11, 1090.
[18] Chen Y. et al. (2016). IBM Watson: How Cognitive Computing Can Be Applied to Big Data Challenges in Life Sciences Research, Clinical Therapeutics, 38, 689.
[19] European Commission. (2020). White Paper On Artificial Intelligence - A European approach to excellence and trust, 2. Available at <https://ec.europa.eu/info/sites/info/files/commission-white-paper-artificial-intelligence-feb2020_en.pdf>.
[20] Mullard, A. (2017). The drugmaker's guide to the galaxy. Nature, 549, 445–447.
[21] Mak, K.K & Pichika M.R. (2019). Artificial intelligence in drug development: present status and future prospects. Drug Discovery Today, 24(3), 773.
[22] Mak, K.K & Pichika, M.R. (2019). Artificial intelligence in drug development: present status and future prospects. Drug Discovery Today, 24(3), 773; *see also* Bishop, C.M. (2013). Model-based machine learning. Philos. Trans. A Math. Phys. Eng. Sci., 371; VoPham, T. et al. (2018). Emerging trends in geospatial artificial intelligence (geoAI): potential applications for environmental epidemiology. Environ. Health, 17, 40; Lee, J.-G. et al. (2017). Deep learning in medical imaging: general overview. Korean J. Radiol., 18, 570–584.
[23] Fleming, N. (2018). How artificial intelligence is changing drug discovery. Nature. Available at <https://www.nature.com/articles/d41586-018-05267-x>.
[24] Mak, K.K & Pichika M.R. (2019). Artificial intelligence in drug development: present status and future prospects. Drug Discovery Today, 24(3), 773.
[25] Smith, S. (2020). 230 Startups Using Artificial Intelligence in Drug Discovery. Available at <https://blog.benchsci.com/startups-using-artificial-intelligence-in-drug-discovery>.
[26] Emig, D. et al. (2013). Drug target prediction and repositioning using an integrated network-based approach. PLoS One 8, e60618; Duch, W. et al. (2007). Artificial intelligence approaches for rational drug design and discovery. Curr. Pharm. Des. 13, 1497–1508.
[27] Hughes, J.P. et al. (2011). Principles of early drug discovery. Br. J. Pharmacol. 162, 1239–1249.
[28] Merk, D. et al. (2018). De novo design of bioactive small molecules by artificial intelligence. Mol. Inform. 37, 1700153.
[29] Klopman, G. et al. (2004). ESP: a method to predict toxicity and pharmacological properties of chemicals using multiple MCASE databases. J. Chem. Inf. Comput. Sci. 44, 704–715.
[30] Menden, M.P. et al. (2013). Machine learning prediction of cancer cell sensitivity to drugs based on genomic and chemical properties. PLoS One 8, e61318.
[31] Nascimento, A.C.A. et al. (2016). A multiple kernel learning algorithm for drugtarget interaction prediction. BMC Bioinf. 17, 46.
[32] Zeng et al. (2020). Target identification among known drugs by deep learning from heterogeneous networks. Chem. Sci., 11, 1775 ('[w]e develop deepDTnet, a deep learning methodology for new target identification and drug repurposing in a heterogeneous drug–gene– disease network embedding 15 types of chemical, genomic, phenotypic, and cellular network profiles. Trained on 732 U.S. Food and Drug Administration-approved small molecule drugs, deepDTnet shows high accuracy (the area under the receiver operating characteristic curve ¼ 0.963) in identifying novel molecular targets for known drugs, outperforming previously published state-of-the-art methodologies').
[33] Mak K.K & Pichika M.R. (2019). Artificial intelligence in drug development: present status and future prospects. Drug Discovery Today, 24(3), 775; Seddon, G. et al. (2012). Drug design for ever, from hype to hope. J. Comput. Aided Mol. Des. 26, 137–150.

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these technologies are changing the process of innovation. AI significantly augments human capabilities, shifting the key stages of the inventive process from human ingenuity and perseverance to the computational powers of AI. This, in turn, may transform biopharmaceutical innovation from the serendipitous and unpredictable field of drug discovery into a more structured, efficient, speedy, and predictable process.[34]

However, while such outputs, if they were produced by a human inventor, would be capable of attracting patent protection, does this mean that inventions created with the assistance of AI should be afforded the same treatment? This article argues that the patent law approaches which were developed to assess human-generated inventions are not suitable for AI-assisted inventions and, therefore, urgent reconsideration is required. In particular, while the issues related to inventorship and ownership of such inventions have been widely discussed and seemingly settled,[35] the question of obviousness remains unresolved.[36] Without changes to the current approaches, the bar for patentability of biopharma and pharma inventions will be set and arguably has already been set,[37] very low, providing patent protection for the outputs routinely generated by AI. This may lead to unjustified monopolies in the medical field, exacerbating the problem of strategic patent accumulation that results in high drug prices and unaffordable access to medicines.[38]

This article will first discuss the current approach to the obviousness of biopharmaceutical and pharmaceutical inventions created by a human and will then explain why this approach is not suitable for the analysis of AI-assisted inventions. In particular, it will examine why the current approach to defining the benchmark of the obviousness analysis, i.e. the person skilled in the art, is not suitable for this type of invention and will provide suggestions on how it can be modified by incorporating an AI tool in the definition of the skilled person. It will further consider what should be the focus of the obviousness analysis and will suggest how it can be readjusted by focusing on the inventive activities of the skilled person, rather than the computational powers of AI. Finally, the article will discuss whether the traditional rationale of unpredictability that underpins the obviousness analysis of biopharmaceutical and pharmaceutical inventions is still relevant for AI-assisted inventions. In this respect, it will consider how the notion of a reasonable expectation of success may be readjusted for this type of invention. The article will conclude with some further suggestions.

1.The traditional approach to the assessment of obviousness

Not every invention deserves a patent. For the invention to be patented, it must meet specific patentability requirements: i.e. it must be new, non-obvious, industrially applicable, and must not fall within the list of excluded subject matters.[39] While each of these requirements bears an important mission, the goal of the inventive step is to ensure that patents are granted to only genuine inventions.[40] It is also the most difficult stage in the patentability assessment as it is based on specific facts of each case and involves, to some extent, subjective judgment of what is or is not obvious.[41] To bring a certain level of objectivity to the assessment of obviousness, patent law relies on a legal fiction by examining the invention through the eyes of the person skilled in the art. The main task at this stage is to demonstrate that the invention is, in fact, a 'step forward, which such a person couldn't have thought of'.[42] The EPO explains that the term 'obvious' means that the claimed invention 'does not go beyond the normal progress of technology but merely follows plainly or logically from the prior art, i.e. something which does not involve the exercise of any skill or ability beyond that to be expected of the person skilled in the art'.[43] A key question, therefore, is whether the invention would have been obvious to the person skilled in the art at the priority date.[44] To answer this question, various jurisdictions have developed different structural approaches.[45] These tests, while different in some respects, share similar elements that need to be established to determine whether the invention is obvious. This includes the identification of the person skilled in the art and his common general knowledge, scope and content of the prior art, differences between the invention and the prior art, and the assessment of whether such differences would have been obvious to the skilled person. The assessment also often takes

[34] Fleming, N. (2018). How artificial intelligence is changing drug discovery. Nature. Available at <https://www.nature.com/articles/d41586-018-05267-x> (citing Niven Narain, Berg's co-founder and chief executive "We are turning the drug-discovery paradigm upside down by using patient-driven biology and data to derive more-predictive hypotheses, rather than the traditional trial-and-error approach').

[35] *See* the decisions by the EPO, the UK IPO and the USPTO on the refusal to accept patent applications that designated an artificial intelligence called DABUS as the inventor. EPO, 'EPO publishes grounds for its decision to refuse two patent applications naming a machine as inventor' (28 January 2020). Available at <https://www.epo.org/news-events/news/2020/20200128.html>; the UK IPO decision BL O/741/19 (04 December 2019). Available at <https://www.ipo.gov.uk/p-challenge-decision-results/o74119.pdf>; the USPTO decision, App'n No. 16/524,350 (22 April 2020). Available at <https://www.uspto.gov/sites/default/files/documents/16524350.pdf>; *see* also Shemtov, N. (EPO, 2019). A study on inventorship in inventions involving AI activity.

[36] See e.g. Ramalho, A. (2018). Patentability of AI-Generated Inventions: Is a Reform of the Patent System Needed? Available at <https://ssrn.com/abstract=3168703>; Block, P. (2017). The inventor's new tool: artificial intelligence – how does it fit in the European patent system? European Intellectual Property Review, 39(2), 69-73; Fraser, E. (2016). Computers as inventors – legal and policy implications of artificial intelligence on patent law. SCRIPTed, 13(3), 305-333; Fabris, D. (2020). From The Phosita To The Mosita - Will "Secondary Considerations" Save Pharmaceutical Patents From Artificial Intelligence? IIC, 52; Abbott, R. (2018). Everything Is Obvious. UCLA L. Rev., 66, 2; Reinbold, P. (2020). Taking Artificial Intelligence Beyond the Turing Test. Wisconsin Law Review, 2020; Hattenbach, B. & Glucoft, J. (2015). Patents in an era of infinite monkeys and artificial intelligence. Stanford Technology Law Review, 19, 32-51; Yanisky-Ravid, S. & Liu, X. (2017). When Artificial Intelligence Systems Produce Inventions: The 3A Era and an Alternative Model for Patent Law. Cardozo Law Review, Forthcoming. Available at <https://ssrn.com/abstract=2931828>.

[37] Fleming, N. (2018). Computer-calculated compounds. Researchers are deploying artificial intelligence to discover drugs. Nature, 557, S55; Iglesias, M., Shamuilia, S., & Anderberg, A. (2019). Intellectual Property and Artificial Intelligence: A literature Review. European Commission, 13.

[38] Gurgula, O. (2017). Strategic Accumulation of Patents in the Pharmaceutical Industry and Patent Thickets in Complex Technologies – Two Different Concepts Sharing Similar Features. IIC, 48(4).

[39] Article 27 of the Treaty on Trade Related Aspects of Intellectual Property Rights, an annex to the World Trade Organisation Agreement (1994); Article 52(1) of the European Patent Convention (2000) (EPC); Article 1(1) of the Patent Act 1977 (as amended).

[40] ibid.

[41] Grubb, P.W. et al. (2016). Patents for Chemicals, Pharmaceuticals, and Biotechnology. Fundamentals of Global Law, Practice and Strategy (6th edn) OUP, 71-72.

[42] Boulet, P. et al (2003). Drug patents under the spotlight**.** Sharing practical knowledge about pharmaceutical patents. Médecins Sans Frontières, para 3.2.

[43] EPO, 'Guidelines for Examination in the European Patent Office' (November 2019 edn), Part G – Chapter VII, Section 4 (*EPO Guidelines*).

[44] ibid.

[45] The EPO applies the so-called 'problem-and-solution approach' (*EPO Guidelines*, Part G – Chapter VII, Section 5). In the UK, the courts rely on a four-step test restated in *Pozzoli v BDMO* [2007] EWCA Civ 588. The US test for determining obviousness comes from *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 86 S.Ct. 684, 15 L.Ed.2d 545 (1966), in which the Supreme Court listed factual inquiries that should be made by the courts when assessing the issue of obviousness.

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into account secondary considerations, such as 'unexpected results', long-felt need, and commercial success.[46]

1.1. Particularities of the obviousness analysis in the field of drug discovery

The obviousness analysis of biopharmaceutical and pharmaceutical inventions has certain peculiarities. Its underlying feature is that this field is generally considered to be unpredictable. For example, as discussed above, one of the most difficult stages in drug discovery is to select a lead compound. Some compounds may have specific properties that may be useful in treating certain diseases. However, it is only through experiments and testing that one can establish whether they are effective and safe, or whether they turn out to have major side effects. It may sometimes be difficult, or even impossible, to predict which of the selected compounds would have such desired effects. Similar considerations apply to other types of biopharmaceutical and pharmaceutical inventions. In such cases, the obviousness assessment may consider whether a specific route, method, or approach would have been obvious to try for the skilled person to arrive at the invention. This means that if a route or method was obvious to try, the skilled person would be motivated to try it.[47] Nevertheless, the result of such a piece of research may not be obvious because there might be an indefinite number of various options to choose from, and the prior art does not provide sufficient guidance on further actions.[48] Therefore, it is important to make a distinction 'between obvious goals - such as to "increase battery life" or "cure cancer" - and obvious *means* of achieving those goals'.[49] An obvious goal will motivate people to try new things, but that doesn't mean the invention is obvious unless ordinary scientists also have obvious means of achieving those goals.[50] Therefore, the 'obvious to try' test is frequently applied in combination with 'a reasonable expectation of success'. As Wolff explains, '[a] "hope to succeed" is merely a wish, whereas a "reasonable expectation of success" presupposes a scientific assessment of facts relevant to the field of the invention at the time of the invention'.[51]

As a result, obviousness may be found when it can be shown that the skilled person would have followed the teaching of the prior art with a reasonable expectation of success.[52] On the other hand, it is often successfully argued that the invention is not 'obvious to try with a reasonable expectation of success' because it is impossible to foresee whether a chosen compound will have the desired properties.[53] Hence, while a specific route may have been 'obvious to try', the results of the research would be perceived by the skilled person as unpredictable and, thus, non-obvious.[54] The application of this test by the EPO, as well as the UK and US courts, will be discussed below.

Therefore, unpredictability is an important factor in the obviousness analysis of biopharmaceutical and pharmaceutical inventions, which is taken into account in various jurisdictions. For example, in a recent EPO case, the Board held that a specific crystalline form of bosutinib monohydrate was non-obvious.[55] While the Board acknowledged that the prior art teaches the investigation of polymorphs to isolate the crystalline form having the most desirable properties, it found, however, that this, in itself, was not sufficient to deny the inventive step. It explained that '[o]nly if the prior art contains a clear pointer that it is the claimed subject-matter that solves this problem or where it at least creates a reasonable expectation that a suggested investigation will be successful can the inventive step be denied'.[56] The Board took the view that since there were no such indications in the prior art, it was entirely unpredictable which crystalline form was the most stable one.[57] In support of its findings, it cited prior art, which stated that 'solvate formation can be a nightmare because it is extremely difficult to predict whether a new species may crystallize from a solution with one or more molecules of solvent'.[58] As a result, it concluded that 'the unpredictability of polymorphism screening does not represent a reasonable expectation that the specific crystalline … would be the most stable form'.[59]

Likewise, both in the UK and US, the unpredictability of the biopharmaceutical and pharmaceutical field is generally perceived by the courts as a feature supporting non-obviousness. Specifically, these jurisdictions have rejected a 'mechanistic application of the "obvious to try" approach'[60] and require a 'reasonable expectation of success' to prove obviousness. In the UK, the rationale for this was neatly explained by Professor Sir Hugh Laddie,[61] who argued that the 'obvious to try' test is irrational and unworkable. He explained that if the reward for finding a solution and obtaining a monopoly is substantial, then it would be reasonable for large

[46] See e.g. *EPO Guidelines*, Part G – Chapter VII, Section 10.1-10.3; *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 86 S.Ct. 684, 15 L.Ed.2d 545 (1966); *Generics (UK) Ltd v H Lundbeck* [2007] RPC 32 at [72].
[47] Lemley, M.A. (2017). Expecting the Unexpected. Notre Dame L. Rev., 92, 1374.
[48] *See e.g.* EPO Case Law of the Boards of Appeal (8th edn, 2016) Chapter I D, para 7.1. (explaining that 'even if it was obvious for the skilled person to try an experiment, it was not necessarily true that this person would have any reasonable expectation of success when embarking on it').
[49] Lemley, M.A. (2017). Expecting the Unexpected. Notre Dame L. Rev., 92, 1374.
[50] ibid.
[51] Wolff, M.E. (2011). Drug discovery market exclusivity after KSR: The challenge to pharmaceutical scientists and the US congress. Journal of Pharmaceutical Sciences, 100(8), 3046.
[52] EPO Case Law of the Boards of Appeal (8th edn, 2016) Chapter I D, para 7.1.
[53] Sullivan, C. & Kline, M. (2016). Introduction to Patentability in Drug Development. Future Science Ltd., 90 ('it is not possible to predict pharmaceutical activity *ab initio*').
[54] Buteau, K. (2010). Deuterated Drugs: Unexpectedly Nonobvious. J. High Tech. L., 10(1), 38; Trask, A.V. (2008). Obvious to Try: A Proper Patentability Standard in the Pharmaceutical Arts. Fordham L. Rev., 76(5), 2665.
[55] T 1684/16 () of 3.3.2020, para 4.3.1.
[56] ibid, para 4.3.4.
[57] ibid, para 4.3.4.
[58] ibid, para 4.3.4.
[59] ibid, para 4.3.4.
[60] *Actavis Group PTC EHF v Eli Lilly & Co*, 2015 WL 6966272 (2015) [105]; see also in Tomlinson's Appn (1966) 363 F 2d 928 at 931 ('[t]here is usually an element of 'obviousness to try' in any research endeavour that is not undertaken with complete blindness but rather with some semblance of a chance of success, and that patentability determinations based on that as the test would not only be contrary to statute but result in a marked deterioration of the whole patent system as an incentive to invest in those efforts and attempts which go by the name of 'research'.)
[61] Sir Hugh Laddie (2004). Patents - what's invention got to do with it? In D. Vaver & L. Bently (Eds.), Intellectual Property in the New Millennium, 91-93, CUP.

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players to investigate all the potential avenues and see if any of those would provide the desired result, despite the prospects of any of them succeeding being potentially less than 50/50. The larger the reward the larger the number of avenues they would be willing to investigate. Consequently, the more valuable the solution is, the more difficult it will be to escape an obvious challenge.[62] Carr J referred to this problem as 'Catch 22', which is inherent for inventions in an empirical art.[63] Therefore, the requirement to demonstrate a reasonable or fair expectation of success is seen as an important policy consideration that takes into account the particularities of medical innovation.[64] Relying on this rationale, many biopharmaceutical and pharmaceutical inventions have been found non-obvious because the prior art did not provide the skilled person with a reasonable expectation of success that a particular route would work. For example, this line of argument was relied upon by the Court of Appeal in *Teva UK v Leo Pharma.*[65] The patents concerned two well-known compounds, calcipotriol and betamethasone, which were previously used individually in the treatment of psoriasis. These two compounds were claimed, in combination with a known solvent called Arlamol E.[66] Jacob LJ held that choosing a particular solvent was inventive.[67] He noted that 'identifying a non-aqueous solvent which would work to produce a stable ointment, was not easy' and that '[f]inding one was a research project'.[68] The reason for this is that 'there was no sufficient expectation of success. Yes, a particular candidate might work, but it was far from certain that it would'.[69]

A similar rationale is followed also in the US. As one of the courts noted when considering the validity of a drug patent, 'unpredictability' is the touchstone of obviousness.[70] In such cases, the Federal Circuit stated that '[a]n "obvious-to-try" situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued'.[71] In *O'Farrell*, the court further provided examples of when it may be 'obvious to try' a certain approach, but the outcome would not be obvious.[72] One such scenario is 'what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful'.[73] The court explained that the finding of obviousness in such a situation based on 'obvious to try' alone, 'specifically penalizes people in areas of endeavor where advances are won only by great effort and expense'.[74] On the other hand, as the Supreme Court explained in *KSR v. Teleflex,*[75] the invention would be obvious because it was obvious to try, if '…there is a design need or market pressure to solve a problem and there are *a finite number of identified, predictable solutions'*, and therefore, 'a person of ordinary skill has good reason to pursue the known options within his or her technical grasp' and it '*leads to the anticipated success'.*[76]

Good examples that demonstrate how this rationale is applied by the US courts are *Pfizer* and *Takeda*. In *Pfizer v. Apotex,*[77] the Federal Circuit found a patent for the besylate salt of amlodipine obvious because there were only a finite number (i.e. fifty-three) of pharmaceutically acceptable salts to be tested for improved properties.[78] The court stated that the person skilled in the art when encountering the problems with the machinability of a compound would have sought to form a salt of the compound and would have been able to narrow the group of potential salt-formers to a group of fifty-three anions known to form pharmaceutically acceptable salts. This would be an acceptable number to form a reasonable expectation of success.[79] On the other hand, in *Takeda v. Alphapharm*,[80] which related to the Type 2 diabetes drug Actos, the court found the invention non-obvious. The claimed compound, pioglitazone, belonged to a large class of drugs known as the thiazolidinediones (TZDs). The Federal Circuit found that the prior art discloses hundreds of millions of TZD compounds, including the structurally close compound b, and nothing suggested to the skilled person to select this compound b as a target for further modification to arrive at pioglitazone.[81] Therefore, referring to the decision in *KSR*, the court stated that '[r]ather than identify predictable solutions for antidiabetic treatment, the prior art disclosed a broad selection of compounds any one of which could have been selected as a

[62] ibid.
[63] *Actavis Group PTC EHF v Eli Lilly & Co*, 2015 WL 6966272 (2015) [106].
[64] *Actavis Group PTC EHF v Eli Lilly & Co*, 2015 WL 6966272 (2015) [103].
[65] [2015] EWCA Civ 779.
[66] ibid, para 10.
[67] ibid, para 40.
[68] ibid, para 24.
[69] ibid; see also *Leo Pharma A/S v Sandoz Ltd* [2009] EWHC 996 (Pat) (where Floyd J rejected the arguments that the motivation was based on the common general knowledge and that it involved routine research procedures).
[70] Valeant Int'l (Barbados) (n 392), at *12.
[71] *In re* Eli Lilly & Co., 902 F.2d 943, 945 (Fed.Cir. 1990).
[72] *In re O'Farrell*, 853 F.2d 894 (Fed.Cir. 1988).
[73] ibid, at 903 (Another scenario occurs when 'what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it').
[74] *In re* Merck & Co., 800 F.2d 1091, 1100 (Fed. Cir. 1986) (Baldwin, J., dissenting); see also Andrew V. Trask, A.V. (2008). Obvious to Try: A Proper Patentability Standard in the Pharmaceutical Arts. Fordham L. Rev., 76(5), 2663.
[75] *KSR v. Teleflex* (n 340), at 1742 (emphasis added).
[76] *KSR v. Teleflex* (n 340), at 1742 (emphasis added).
[77] *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 82 USPQ2d 1321 (Fed. Cir. 2007).
[78] ibid, at 1363, 1367
[79] ibid, at 1363. See also *In re Kubin*, 561 F.3d 1351, 90 USPQ2d 1417 (Fed. Cir. 2009) (The Board noted that the problem facing those in the art was to isolate a specific nucleic acid, and there were a limited number of methods available to do so. The Board concluded that the skilled artisan would have had reason to try these methods with the reasonable expectation that at least one would be successful).
[80] *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 83 USPQ2d 1169 (Fed. Cir. 2007).
[81] ibid, at 1357-1358.

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lead compound for further investigation'.[82] Consequently, it was not 'obvious to try'.[83] Moreover, the court noted that, even if it was possible to establish that the skilled person would have been motivated to select compound b, nothing in the prior art would have prompted him to make the specific molecular modifications to synthesize the claimed compound and, therefore, there was no expectation of success.[84]

The case law developed by the EPO, the UK, and US courts demonstrates how the notion of the unpredictability of the biopharmaceutical and pharmaceutical field influences the assessments of obviousness. The absence of some incentives or motivation in the prior art that would trigger the interest of the skilled person to pursue a specific avenue and his inability to predict in advance without clear guidance from the prior art of whether the chosen route would have desired results would typically support non-obviousness. Furthermore, a small number of potential avenues that exist in the prior art may be indicative of obviousness because it would be possible for the skilled person to investigate all of them.[85] However, the fact that the prior art discloses a large number of avenues and provides no clear guidance for the skilled person on which to choose may support a non-obvious finding.[86] This is because it would be extremely difficult for the skilled person to analyze all the options to arrive at the invention. All these considerations reflect the reality of conventional drug discovery, which is typically fraught with uncertainty and unpredictability, may contain numerous potential avenues for research and little certainty in their successful outcome. Therefore, the current approach to the obviousness of biopharmaceutical and pharmaceutical inventions is aimed at incentivizing innovation in this field by granting patent protection to inventions resulting from unpredictable research projects, in which the ordinary skilled person would have no reasonable expectation of success based on the prior art. Such inventions may be the results of human ingenuity and perseverance or even mere serendipity or chance that a human inventor stumbles upon by sheer luck. On the other hand, patent law refuses patent protection to any invention that 'merely follows plainly or logically from the prior art, i.e. something which does not involve the exercise of any skill or ability beyond that to be expected of the person skilled in the art'.[87] Therefore, the results of routine research activities by the skilled person would not be patentable. The rationale of this approach to obviousness is firmly based on the notion of an inventive process undertaken by a human who employs his or her capabilities and knowledge of the field to arrive at the invention. However, as will be argued further, this approach that has proven to be a useful tool in assessing inventions made by a human may not be suitable for analyzing inventions that were created with the assistance of AI and, thus, requires certain adjustments.

2. Readjusting the obviousness analysis for AI-assisted inventions

As can be seen from the above discussion, the obviousness analysis is deeply rooted in the capabilities of a human inventor. However, AI significantly expands the range of things that a human aided by AI can discover without undue effort or experiment.[88] For example, IBM Watson, a cognitive computing technology, was used by a large biopharmaceutical company to identify compounds in the company's existing therapeutic portfolio that could be potential candidates to treat malaria.[89] Watson reviewed the MEDLINE literature, which contains >24 million published medical and scientific articles with 1.8 million new articles published annually,[90] exploring all drugs approved for use in humans and searched for statements suggesting efficacy against the malaria parasite.[91] Then, Watson analyzed all the existing compounds in the company database to identify any that had a structural similarity to known malaria treatments by looking for similarities in chemical structure and mechanisms of action.[92] It suggested 15 drug candidates from the company's existing portfolio as potential antimalarial drugs; this process took less than 1 month.[93] To compare, the company had been working on this project with at least 10 research scientists for more than 14 months and had identified a similar number of candidates.[94] However, while half of the candidates generated by the company and Watson were the same, the rest on the list produced by the latter were candidates that the researchers had not identified during their research.[95]

This shows that many AI-assisted inventions may be the result of a massive computational power that allows for rapid trial and error searching - something that an AI system can be programmed to do, while from the perspective of a skilled person without the aid of AI, the results may be surprising.[96] Therefore, if the current obviousness analysis is to be applied to AI-assisted inventions, human capabilities would be judged against AI capabilities. This would set a very low

[82] ibid, at 1358.
[83] ibid, at 1359.
[84] ibid, at 1363; see also *Valeant Pharmaceuticals Int'l Inc. et al. v. Mylan Pharm. Inc.*, case number 18-2097 (8 April 2020), p 16.
[85] *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 82 USPQ2d 1321 (Fed. Cir. 2007).
[86] *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 83 USPQ2d 1169 (Fed. Cir. 2007).
[87] *EPO Guidelines*, Part G – Chapter VII, Section 4.

[88] Vertinsky, L. (2018). Thinking Machines and Patent Law. In W. Barfield & U. Pagallo (Eds.). Research Handbook of Artificial Intelligence (Edward Elgar Publishing), 503.
[89] Chen Y. et al. (2016). IBM Watson: How Cognitive Computing Can Be Applied to Big Data Challenges in Life Sciences Research, Clinical Therapeutics, 38, 698.
[90] ibid; NIH U.S. (2015). National Library of Medicine MEDLINEs Fact Sheet. Available at <https:// www.nlm.nih.gov/pubs/factsheets/ medline.html>.
[91] Chen Y. et al. (2016). IBM Watson: How Cognitive Computing Can Be Applied to Big Data Challenges in Life Sciences Research, Clinical Therapeutics, 38, 698.
[92] ibid.
[93] Lohr, S. (2013). And now, from I.B.M., Chef Watson. New York Times. Available at <http://www.nytimes. com/2013/02/28/technology/ibm-exp loring-new-feats-for-watson.html?_r=0>.
[94] ibid.
[95] ibid.
[96] **Vertinsky, L. (2018).** Thinking Machines and Patent Law. In W. Barfield & U. Pagallo (Eds.). Research Handbook of Artificial Intelligence (Edward Elgar Publishing), 503.

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patentability standard as many AI-assisted inventions may be non-obvious to the skilled person. As a result, this may lead to patent flooding, as it may be relatively easy to obtain patent protection for inventions that are routinely generated by AI. This section will, therefore, discuss some possible ways of readjusting the obviousness assessment that could be applied to AI-assisted inventions. For this, two main questions will need to be answered: (a) what should be the characteristics of the 'person skilled in the art' for AI-assisted inventions?, and (b) what is the focus of the obviousness analysis about such inventions. It is believed that the answers to these questions will allow for an adequate readjustment of the obviousness analysis that will provide a fair balance between the monopoly granted to the owners of AI-assisted inventions and society.

2.1. The person skilled in the art

A key benchmark against which obviousness is judged is the 'person skilled in the art'. This is a fictional legal concept that is aimed at providing an objective test for the assessment of obviousness. Therefore, proper identification of the skilled person and his characteristics may have important consequences.[97] This is because everything or alternatively nothing will be obvious to an incorrectly identified skilled person.[98] A skilled person is typically defined as an expert in a relevant field who has average knowledge and ability but is not exceptional, outstanding, or brilliant.[99] Such a person must be neither over- nor under-qualified and is deemed to be uninventive.[100] This raises a difficult question of how to define an appropriate benchmark for AI-assisted inventions and whether/how the current standard should incorporate AI. The following sections will explain in more detail some of the difficulties of applying the current approach to defining the skilled person and will suggest an alternative approach.

2.1.1. Is AI a tool or an inventor?

Before moving forward with the discussion, it is first necessary to answer one key question: should AI be perceived as an inventor or as a tool available to the skilled person? While AI may play a decisive role in the inventive process of drug discovery, it has not reached the level of advancement that would allow researchers to merely insert some general instructions, e.g. 'invent a cancer drug', in response to which AI would generate a list of proposals of breakthrough medicines. As was discussed above, the process of drug discovery is very complex; it includes a number of stages, each of them requires making decisions and subjective human judgment. The role of AI in this process is to make the analysis of a vast amount of data more efficient. This is conducted under the direction of researchers who design instructions, select input data, and validate the outcomes. Therefore, while such technologies significantly reduce the time and efforts that researchers need to invest in drug discovery, they should be considered as tools in the disposal of researchers, and not independent inventors.

2.1.2. Has AI become a 'normal' tool in the biopharmaceutical field?

According to the EPO Guidance, the average skilled person is presumed to have at his disposal 'the means and capacity for routine work and experimentation which are normal for the field of technology in question'.[101] This raises the question of whether AI technology has become a 'normal' tool for routine work in the relevant field of technology, and, in particular, in drug discovery.[102] It seems that while the use of AI technologies is becoming more widespread, it is unlikely that today it has reached the level of a normal tool for the routine work and experimentation available for scientists at all stages of drug discovery.[103] This, potentially, means that AI would not be taken into account in the assessment of biopharmaceutical and pharmaceutical inventions, even if these inventions were in fact created with the assistance of AI.[104] However, as was noted earlier, more and more inventions are created with the assistance of AI (and, arguably, this number will continue to grow).[105] Some stages of drug discovery, such as target identification and validation, safety tests, compound discovery, and lead optimization, are already heavily employing AI.[106] Therefore, the obviousness analysis should take into account the advancement of AI technology in these areas of drug discovery. Without the relevant changes to the obviousness, the bar for such inventions would be set at a very low level, which may render the majority of inventions created with the assistance of AI non-obvious to the skilled person who relies only on their common general knowledge, mental capabilities, and non-AI technology.

2.1.3. Unlike other tools, AI is capable of being 'inventive'

To establish an objective standard of obviousness, the skilled person is considered to be unimaginative and

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97 Birss, C. et al. (2020). Terrell on the Law of Patents (19th Edn.). Sweet & Maxwell, para 8-02 and para 8-25.

98 CIPA. (2019). CIPA Guide to the Patents Acts (9thEdn.) Sweet & Maxwell, para 3-07; *Actavis UK Ltd v Merck & Co Inc [2007] EWHC 1311 (Pat)*.

99 see *T 39/93 ALLIED COLLOIDS/Polymer powders OJ EPO 1997, 134* at 7.8.4

100 CIPA. (2019). CIPA Guide to the Patents Acts (9thEdn.) Sweet & Maxwell, para 3-07; *Pfizer's Patent [2001] F.S.R. 20.*

101 *EPO Guidance*, G-VII.3.

102 *EPO Guidelines*, Part G – Chapter VII -3.; in the US, the Federal Circuit stated in *Environmental Designs, Ltd. v. Union Oil Co*, 713 F.2d 693 (1983) that the level of ordinary skill in the pertinent art is defined taking into account several factors, including 'sophistication of the technology'.

103 Fleming, N. (2018). How artificial intelligence is changing drug discovery. Nature, **557**, S55-S57 ('Despite these promising applications, many scientists are unaware of the capabilities of AI'). Available at <https://www.nature.com/articles/d41586-018-05267-x>; Smith, S. (2018). 6 Things We Learned about Artificial Intelligence in Drug Discovery from 330 Scientists. (A survey on AI in drug discovery undertaken by BenchSci in 2017 showed that only 15% of scientists who took part in the survey were very familiar with AI,
44% were somewhat familiar with AI, and more than 40% were unfamiliar with AI) Available at <https://blog.benchsci.com/6-things-we-learned-about-artificial-intelligence-in-drug-discovery-from-330-scientists>.

104 Chen Y. et al. (2016). IBM Watson: How Cognitive Computing Can Be Applied to Big Data Challenges in Life Sciences Research, Clinical Therapeutics, 38.

105 Ramalho, A. (2018). Patentability of AI-Generated Inventions: Is a Reform of the Patent System Needed? Available at <https://ssrn.com/abstract=3168703>.

106 Smith, S. (2018). 6 Things We Learned about Artificial Intelligence in Drug Discovery from 330 Scientists. ('among scientists whose organizations use AI, the focus is heavily on target identification and validation, safety tests, compound discovery, and lead optimization'.)

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uninventive.[107] The current legal construct of a notional skilled person, therefore, is designed in such a way as to help to remove the inventive potential that most real people have.[108] For example, the inventor himself may not be considered to be a relevant skilled person.[109] In *ALLIED COLLOIDS/Polymer powders,* it was held that the inventor is set apart from the average skilled person because he/she is possessed of inventive capability, whereas the notional skilled person is not.[110] This complicates the exercise of establishing an appropriate standard for AI-assisted inventions. While AI is perceived as a tool at the disposal of the skilled person, what makes it different from any other type of tool is its ability to generate the solutions which, from the perspective of the skilled person without AI, may be considered as 'inventive'. AI can learn and act accordingly: it is constantly evolving and improving.[111] Unlike other tools, AI technologies are capable of more independent and creative actions than merely following the instructions of researchers. This poses a difficulty in establishing an objective standard since, as was noted, the skilled person is perceived as uninventive.

2.1.4. The skilled person is a specialist in the field of the invention

A patent specification is addressed to those persons likely to have a practical interest in the subject matter of the invention.[112] Such persons will have practical knowledge and experience of the kind of work in which the invention is intended to be used.[113] For example, in *Takeda* (a patent for a new chemical compound) the ordinary person skilled in the art would have a graduate degree in chemistry and practical experience applying that education by working at or consulting with a pharmaceutical company in the development of pharmaceutical compounds.[114] Also, although the skilled person is a hypothetical construct, its composition and mind-set are founded in reality.[115] Therefore, as inventions in life sciences are typically the work of teams of inventors, the state of the art can also be assessed for obviousness through the eyes of such a team having different skills.[116] For example, in *Actavis v ICOS Corp*, the validity of a patent to a particular dosage regime was judged through the eyes of the skilled team that included a clinical pharmacologist and a clinician.[117] Considering the current practice of defining the skilled person/team to assess the obviousness of medical inventions, it is unclear whether an AI specialist would be included in such a team.

2.2. Proposal for a new standard for defining the skilled person in the obviousness assessment of AI-assisted inventions

To overcome the difficulties discussed above, this article suggests the following approach for defining the skilled person, which, it is believed, will provide an objective standard for the obviousness assessment of AI-assisted inventions. *First*, it submits that AI should be perceived as a tool, albeit a sophisticated one, not an autonomous inventor, and should be incorporated into the characteristics of the skilled person. *Second*, to properly define the characteristics of the skilled person, such a person should be equipped with or have access to an equivalent AI used in the inventive process, or if such information is not disclosed by the applicant, with the best AI available in the relevant field.

More specifically, to establish an objective benchmark for the assessment of AI-assisted inventions, this article argues that the skilled person should be equipped with or have access to AI. The EPO Guidance, as discussed above, provides that the skilled person has at his disposal 'the means and capacity … which are normal for the field of technology in question'.[118] Therefore, according to this approach, the skilled person should be equipped with AI which is normal for the field of technology of the invention. However, it may be difficult to define objectively what constitutes a 'normal AI',[119] as it may depend on various factors, including specific algorithms and data used to train it, which may impact on the level of the 'skills' of AI. To provide more objectivity to the standard, two alternatives may be considered. First, the skilled person may be equipped with an equivalent AI technology that has been used to achieve a claimed invention. For this, the applicant would need to disclose the details of the AI used in the inventive process. The difficulty with this approach is that, currently, the disclosure of how the invention is achieved is not required.[120] This is because the analysis is focused on the result, i.e. the invention, and not on the inventive process.[121] An alternative option which may avoid the

[107] *Generics (UK) Ltd & Ors v H Lundbeck A/S* [2007] EWHC 1040 (Pat); [2007] R.P.C. 32 [36] (the person skilled in the art ..'is unimaginative and has no inventive capacity'); the US Supreme Court in *KSR v. Teleflex* 550 U.S. 398, 421 (2007) referred to the skilled person as, someone who has 'ordinary creativity'. In the EPO, the person skilled in the art is also deemed to lack creative thinking and inventive imagination (*EPO Guidelines*, Part G, Ch VII, Section 3)

[108] *Clearswift Ltd v Glasswell (IP) Ltd [2018] EWHC 2442 (Pat)* at [34].

[109] *Wellcome Foundation v VR Laboratories [Australia] [1982] R.P.C. 343*

[110] T 39/93 Polymer powders/ALLIED COLLOIDS LIMITED of 14.2.1996.

[111] Shlomit Y.-R., & Liu, X. (2017). When Artificial Intelligence Systems Produce Inventions: The 3A Era and an Alternative Model for Patent Law. Cardozo Law Review, 39, 2215-2263. Available at <https://ssrn.com/abstract=2931828>; European Commission (2018). Artificial intelligence, real benefits. Available at <https://ec.europa.eu/digital-single-market/en/news/artificial-intelligence-real-benefits>.

[112] See e.g. *Actavis Group PTC EHF v Eli Lilly & Co*, 2015 WL 6966272 (2015) [7] citing *Catnic v Hill and Smith* [1982] RPC 183 at 242 per Lord Diplock.

[113] Birss, C. et al. (2020). Terrell on the Law of Patents (19th Edn.). Sweet & Maxwell, para 8-29; CIPA. (2019). CIPA Guide to the Patents Acts (9thEdn.) Sweet & Maxwell, para 3-07.

[114] *Takeda Chemical Industries, Ltd. v. Mylan Labs*., 417 F. Supp. 2d 341 (S.D.N.Y. 2006), at 373.

[115] *Actavis Group PTC EHF v Eli Lilly & Co*, 2015 WL 6966272 (2015) [7] citing Schlumberger v Electromagnetic Geoservices [2010] EWCA Civ 819; [2010] RPC 33 at [42] per Jacob LJ.

[116] Birss, C. et al. (2020). Terrell on the Law of Patents (19th Edn.). Sweet & Maxwell, para 8-36.

[117] ibid, para 8-41.

[118] *EPO Guidance*, G-VII.3.

[119] Block, P. (2017). The inventor's new tool: artificial intelligence – how does it fit in the European patent system? European Intellectual Property Review, 39(2), 71.

[120] *See e.g.* the last sentence of 35 U.S.C. Section 103(a), which says that '[p]atentability shall not be negated by the manner in which the invention was made'; Block, P. (2017). The inventor's new tool: artificial intelligence – how does it fit in the European patent system? European Intellectual Property Review, 39(2), 70 ('under European patent law 'the way in which an invention has been realised is irrelevant to the question of patentability').

[121] Bently, L. et al (2018). Intellectual Property (5th edn) OUP, 582; See, however, Hattenbach, B. & Glucoft, J. (2015). Patents in an era of infinite monkeys and artificial intelligence. Stanford Technology Law Review, 19, 44 (who argue that the aim of the last phrase of Section 103 is 'to direct courts to disregard whether an invention was conceived in a "eureka" moment or through

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difficulty of establishing a 'normal AI' in the relevant field, as well as the controversies with the requirement to disclose a specific AI used in the inventive process, is to equip the skilled person with the best AI technology that is available in a relevant field. Such an approach can find support in the speech by Mustill LJ in *Genetech,*[122] in which the invention was achieved utilizing genetic engineering using a particular route of recombinant DNA technology, a very new development at that time.[123] The judge noted that:

> *The question of equipment is more puzzling, largely, I believe, because traditional patent law, and, indeed, the current legislation, is ill at ease with this type of complex and rapidly developing new technology. It seems to me, however, that since we are looking to distinguish the inventive spark from a triumph of the method, we 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.*[124]

While each of these approaches may have certain pitfalls, these suggestions aim to remove uncertainties about the computational powers of AI, shifting the focus of the standard for the obviousness assessment to the skills and knowledge that the skilled person relies upon to arrive at the invention with the use of AI.

It is further necessary to consider the composition of the skilled team, its skills, and common general knowledge.[125] While the specialists that would typically be included in a national team to assess medical inventions would know the field of invention and a standard technology employed in such a field, the use of AI will require a new set of skills, i.e. knowledge of how AI systems operate in the process of drug discovery and development. This raises the question of whether the skilled team would include an AI expert. The composition of the skilled team is a question of fact in each case, and is decided with regard 'to the reality of the position at the time' and 'the combined skills (and mind-sets) of real research teams in the art'.[126] Thus, for some projects, an AI expert may be included in the skilled team from the outset. In other cases, the national team may invite an AI expert to overcome some difficulties they have encountered along the way.[127] In such cases, it would be necessary to establish an AI expert's level of skills, his common general knowledge related to AI systems, and their application in drug discovery or, more narrowly, in a specific area of drug discovery.

2.2.1 Assessing obviousness of AI-assisted inventions

Once an appropriate benchmark for the obviousness assessment is set, the next stage is to understand what the law means/should understand concerning 'the inventive step' or 'obviousness' about the inventions created with the assistance of AI. This question requires answering some further inquiries. First, what should the focus of the obviousness assessment of such inventions be, considering that it is the inventive activities of a human that should be assessed, rather than the computational powers of AI? Second, is the rationale that underlines the current approach to the assessment of biopharmaceutical and pharmaceutical inventions still good for the AI-assisted invention?

2.2.2 Obviousness of what?

The key question of the obviousness analysis is whether the invention would have been obvious to the person skilled in the art. Therefore, the focus of the analysis is the result – the invention and its obviousness to the skilled person. This is because, '[t]he objective nature of the [obviousness] inquiry means that the actual process by which the invention came about is irrelevant' and, therefore, 'it does not matter if an invention arose as a result of years of research by a team of leading experts, or as a chance result by an unskilled person'.[128] The only thing that matters is 'whether the person skilled in the art would consider the invention to be non-obvious'.[129] In such cases, assessing through the eyes of the person skilled in the art, the obviousness inquiry will examine various elements and factors, including the (closest) prior art relevant to 'the field of endeavor',[130] starting points, motivation to pursue certain routes restricted by the abilities of the skilled person to analyze only a limited amount of options, prejudices, 'mind-set', etc. Moreover, as was discussed above, the analysis will also consider whether the skilled person would have been able to predict in advance a successful outcome with a reasonable expectation of success.

All these factors related to the obviousness analysis have evolved around the 'person' skilled in the art and his

random success'. Its aim was 'to address the process of invention undertaken by human inventors, not machines'.)

[122] *Genentech Inc's Patent (Human Growth Hormone),* [1989] R.P.C. 147 (1988) (this case involved recombinant DNA technology that was a very new development at the time of the invention).

[123] ibid.

[124] ibid, at *278.

[125] *EPO Guidelines*, G-VII at 3 (a skilled person has the common general knowledge and a capacity for routine work and experimentation). See also CIPA. (2019). CIPA Guide to the Patents Acts (9thEdn.) Sweet & Maxwell, para 3.08 referring to *Valensi v BRC [1973] R.P.C. 337* at 377, where the courts stated that the hypothetical addressee is not to be expected to exercise any invention nor any prolonged research enquiry or experiment. He must however be prepared to display a reasonable degree of skill and common knowledge of the art in making trials and to correct obvious errors if a means of correcting them can readily be found.

[126] *Schlumberger Holdings Ltd v Electromagnetic Geoservices AS* [2010] EWCA Civ 819; [2016] R.P.C. 33 at [41].

[127] The latter approach was accepted in *Pfizer Ltd's Patent [2001] F.S.R. 16* at [67], in which *the validity of a pharmaceutical patent was in dispute.* While both parties agreed that the relevant fields of expertise would encompass pharmacology, medicinal chemistry and urology, there was a disagreement of whether the notional team would also include a skilled but unimaginative worker in the PDE field (phosphodiesterases). It was accepted that one should consider the notional team's reaction to the prior art item by item, but bearing in mind that if the art specifically flags a technology in which they would regard themselves as inadequately skilled, they would consider getting help from someone else.

[128] Bently, L. et al (2018). Intellectual Property (5th edn) OUP, 582.

[129] ibid.

[130] *EPO Guidelines*, Part G, Chapter VII-5; CIPA. (2019). CIPA Guide to the Patents Acts (9thEdn.) Sweet & Maxwell, para 3.06; the USPTO Manual of Patent Examining Procedure, Ninth Edition, Revision 10.2019, para 2141 Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 [R-10.2019].

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capabilities. For example, when examining the obviousness of a new lead compound selected from a database of millions of compounds, such factors as a lack of clear directions in the prior art to select a starting point and guidance on its further modification to arrive at a claimed compound would result, as in *Takeda*, in finding such an invention non-obvious. However, these factors become less relevant for AI-assisted inventions. This is because, such inventions will depend upon the configured algorithms, data supplied for the analysis and patterns uncovered in that data, rather than emanating from the prior art, the motivation of AI to select a specific starting point or its reasonable expectation of success.[131] The computation power and data allow AI to analyze and discover hidden patterns, which significantly increases the number of solutions it can consider and reject before arriving at an optimal output.[132] Therefore, applying the same considerations to AI-assisted inventions in the same manner as to non-AI-assisted inventions 'would likely lower the non-obviousness bar and grant the AI too much credit for its abilities'.[133]

This raises an important question of what is it that must not be obvious in the context of AI-assisted inventions to establish the inventive step? As was discussed above, the patent system has evolved around the human inventor and its goal is to incentivize and reward human inventiveness rather than the computational power of AI. It is, therefore, suggested in this article that the obviousness analysis should shift from the result to the activities of the skilled person/team that has led to such a result. Thus, once the skilled person has been defined and equipped with an AI tool, the question should then be, if such a skilled person, looking towards the goal, whether or not it is precisely identifiable in advance, would be able to achieve a successful result.[134]

2.2.3. Is the rationale of obviousness for the analysis of biopharmaceutical and pharmaceutical inventions still good?

The underlying rationale of the obviousness assessment of biopharmaceutical and pharmaceutical inventions, as was discussed above, is that this field is uncertain and unpredictable as it is only through experiments and trials one can establish whether the desired effect will be achieved. It is considered that the patent monopoly is justified because such research is very time-consuming and expensive, and the success rate is low. Therefore, 'if a sufficient reward is not given in those instances where the research bears fruit, the industry will not attract the venture capital which it needs for survival, the research will cease, and humanity will continue to suffer.'[135] This policy rationale is further explained by Kitchin LJ in the often-cited statement in *Medimmune v Novartis*, who noted that:

> *there are areas of technology such as pharmaceuticals and biotechnology which are heavily dependent on research, and* where workers are faced with many possible avenues to explore but have little idea if anyone of them will prove fruitful. *Nevertheless, they do pursue them in the hope that they will find new and useful products. They plainly would not carry out this work if the prospects of success were so low as not to make them worthwhile. But the denial of patent protection in all such cases would act as a significant deterrent to research. (emphasis added).*[136]

Therefore, the core of the current policy is that the successful outcome should deserve a patent monopoly because it is the result of empirical unpredictable research that needs to be incentivized. As the Federal Circuit noted, until the science has advanced to the level when it is possible to predict 'with some minimal reliability' the property and therapeutic value of a researched compound, the result will be considered inventive.[137]

Indeed, until recently, the process of drug discovery has been mostly serendipitous and unpredictable. Many breakthroughs in medical science have been achieved by fortuitous discoveries; this includes penicillin, warfarin, and the smallpox vaccine.[138] As many as 24% of all drugs have been serendipitous discoveries.[139] Such discoveries are often the result of connections randomly made when seemingly different matters were accidentally linked together,[140] which then provide a valuable insight leading to finding new drugs or new uses of existing drugs. For instance, a famous example of the latter is Viagra. Its unintended properties beneficial for treating erectile dysfunction were discovered by chance when conducting trials for a new drug originally aimed at treating cardiovascular diseases.[141] However, the use of AI technology in drug discovery significantly increases the predictability of the research outcomes. Today AI allows researchers to rely more on **science** and less on luck by designing purposeful research which helps to reduce the time and expense involved in developing new treatments.[142] AI technologies can be programmed to make cross-domain linkages instead of relying on serendipity.[143] Based on the 'big data' available today and powerful computers programmed with sophisticated algorithms

[131] Reinbold, P. (2020). Taking Artificial Intelligence Beyond the Turing Test. Wisconsin Law Review, 2020, 23.
[132] ibid.
[133] ibid.
[134] *Genentech Inc's Patent (Human Growth Hormone)* [1989] R.P.C. 147 (1988) [275].
[135] ibid, at [269].
[136] *Medimmune Ltd v Novartis Pharmaceuticals UK Ltd* [2012] EWCA Civ 1234 at [90].
[137] *Eli Lilly & Co., Inc. v. Generix Drug Sales, Inc*., 460 F.2d 1096, 1103 (5th Cir. 1972); *see* also Yoshitani, R.S. & Cooper, E.S. (2007). Pharmaceutical Reformulation: The Growth of Life Cycle Management. HOUS. J. HEALTH L. & POL'Y, 7, 388-405.
[138] Chen Y. et al. (2016). IBM Watson: How Cognitive Computing Can Be Applied to Big Data Challenges in Life Sciences Research, Clinical Therapeutics, 38, 695; Ban, T.A. (2006). The Role of Serendipity in Drug Discovery. Dialogues Clin Neurosci., 8, 335–344; Hargrave, T.E., Bo, Y., & Johannes, R. (2012). Serendipity in Anticancer Drug Discovery. World J Clin Oncol, 3, 1–6.
[139] ibid.
[140] Chen Y. et al. (2016). IBM Watson: How Cognitive Computing Can Be Applied to Big Data Challenges in Life Sciences Research, Clinical Therapeutics, 38, 695.
[141] Osterloh, I.H. (2004). The discovery and development of Viagra ® (sildenafil citrate). In U. Dunzendorter (Ed.), Sildenafil (pp. 1-13). Birkhauser Verlag/Switzerland.
[142] Swartz, A. (2018). Drug discoveries rely less on luck and more on tech. The Washington Post. 05/14/2018.
[143] Chen Y. et al. (2016). IBM Watson: How Cognitive Computing Can Be Applied to Big Data Challenges in Life Sciences Research, Clinical Therapeutics, 38, 695.

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to analyze it, it is now possible to make highly accurate predictions in the area of drug discovery: e.g. how likely one drug may be used in treating another condition.[144]

What does this mean for the assessment of obviousness? Would a prediction by AI be sufficient to establish an expectation of success, especially in circumstances when the algorithm keeps making the right predictions?[145] The answer would probably lie in the required level of expectation that needs to be demonstrated in a given case. What is important, however, is that the showing of absolute certainty of success is not required. Neither the EPO nor the courts in the UK or US require such absolute certainty of success. For example, the EPO Guidelines acknowledge that the skilled person, even when applying routine methods, will not be certain of succeeding.[146] It explains that a lack of an inventive step may be found not only in circumstances where the outcome is predictable but also when there is a reasonable expectation of success.[147] Moreover, it states that while uncertainty is inherent to biological experiments, the skilled person would have no reason to have a skeptical attitude.[148] There would be either some expectation of success or at least a 'try and see' approach, which is not the same as the absence of a reasonable expectation of success.[149] Likewise, in the US, the court in *O'Farrell* stated that '[o]bviousness does not require absolute predictability of success. Indeed, for many inventions that seem quite obvious, there is no absolute predictability of success until the invention is reduced to practice'.[150] A similar approach is followed in the UK.[151] Therefore, the required standard is a 'reasonable' or 'fair' expectation of the skilled person that a particular route of research may lead to a positive result. It could be argued that the use of AI in a research project may provide, in certain circumstances, this 'minimal reliability'[152] sufficient to establish a reasonable expectation of success.

Moreover, the use of AI may significantly change the meaning of a reasonable expectation of success. If currently, to demonstrate such a reasonable expectation of success, it is necessary to show that the prior art has provided some grounds to the skilled person for such an expectation, the use of AI may change this perception dramatically. In particular, with the use of AI, a reasonable expectation of success may also be found in situations previously considered to be the prime examples of non-obviousness. For instance, this technology may affect the understanding of scenarios given in *O'Farrell* discussed earlier. The skilled person with the use of AI would be able, without any difficulties, 'to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful'.[153] As was noted earlier, AI-assisted inventions stem from the computational powers of AI, its specific algorithms and data, rather than from the prior art.[154] As a result, AI technology significantly elevates the level of an expectation of success.[155] It could be argued that the use of AI in some cases may provide grounds for establishing a *prima facie* reasonable expectation of success. In such cases, it would be necessary for the patentee to rebut such a presumption by showing the absence of such an expectation.

Finally, when assessing the activities of the skilled person that uses AI, it would be necessary to examine whether the invention is achieved by inventive activities or routine research. In particular, while the design of a research project with the use of AI may require a lot of effort, expertise, financial resources, necessary equipment, and supplies, is it the kind of activity which, in law, amounts to an inventive step?[156] Despite the process of searching for a new drug being lengthy and expensive, the use of AI in this process may be seen as a routine activity and, thus, the results of such activities may be obvious.[157] For example, Floyd LJ noted in *Actavis v ICOS* that 'a patent will not be granted for an invention which, though not obvious in this *a priori* sense, is nevertheless an invention which would be arrived at by a line of routine and uninventive inquiry which would be carried out by a skilled team'.[158] Therefore, to prove non-obviousness in such cases it may be necessary to demonstrate that the skilled person would require, for example, to overcome some difficulties in a non-obvious way to arrive at the results and/or would have to undergo certain non-obvious steps about the output to improve it. Otherwise, as the court in *Genentech* noted '[i]t may be that such labor and the resulting success deserve a prize, but the law … calls for something more.'[159] The goal of the patent system is to reward inventions, which is something that the ordinary skilled person relying on available tools, including AI technology, would not have created.[160] If the person skilled in the art would have been able to achieve such a result by using AI, the outcome of such an endeavor is the result of ordinary scientific research and not an inventive activity.[161]

3. Concluding remarks and policy considerations

The conventional process of drug discovery is very lengthy, complex, and expensive due to its unpredictable nature. Today, AI has the potential to revolutionize this

144 Swartz, A. (2018). Drug discoveries rely less on luck and more on tech. The Washington Post. 05/14/2018.
145 Finnie, P.J. (2018). AI-generated in silico data in patent applications. Drug Discovery Today, 23(10), 1693.
146 EPO Case Law of the Boards of Appeal (8th edn, July 2016) Chapter I D, para 7.1.
147 ibid.
148 ibid, para 7.2.
149 ibid.
150 *In re O'Farrell*, 853 F.2d 894 (Fed.Cir. 1988) at 903.
151 *See e.g. Novartis AG v Generics (UK) Ltd (trading as Mylan)* [2012] EWCA Civ 1623 [55].
152 *Eli Lilly & Co., Inc. v. Generix Drug Sales, Inc*., 460 F.2d 1096, 1103 (5th Cir. 1972).
153 *In re O'Farrell*, 853 F.2d 894 (Fed.Cir. 1988) at 903.
154 Reinbold, P. (2020). Taking Artificial Intelligence Beyond the Turing Test. Wisconsin Law Review, 2020, 23.
155 Simon, B.M. (2013). The implications of technological advancement for obviousness. Michigan Telecommunications and Technology Law Review, 19, 131 ('In many technological fields, as access to enhanced processing capabilities and information increases, the reasonable expectation of success would also become stronger, particularly in fields with some level of predictability').
156 *Genentech Inc's Patent (Human Growth Hormone)* [1989] R.P.C. 147 (1988) at [273].
157 *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 82 USPQ2d 1321 (Fed. Cir. 2007).
158 *Actavis Group PTC EHF v ICOS Corp* [2017] EWCA Civ 1671; (2018) 159 B.M.L.R. 108 at [156].
159 Genentech Inc's Patent (Human Growth Hormone), [1989] R.P.C. 147 (1988) at [280].
160 Lemley, M.A. (2017). Expecting the Unexpected. Notre Dame L. Rev., 92, 1370.
161 ibid.

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process. It has been increasingly employed at all stages of drug discovery, starting from target identification and the selection of hits, and leads to designing clinical trials. All these stages were previously fraught with uncertainly and serendipity. AI can remove this uncertainty by accurately predicting results and enabling researchers to make decisions based on scientific evidence. As AI significantly expands human capabilities, inventions that were previously the result of human ingenuity, perseverance or serendipity can now be achieved by routine experimentations with the use of AI. What does this mean for patent law? This means that the approaches developed around a human inventor need to be re-examined as, otherwise, results of routine activities generated by AI will be credited with unjust patent monopoly. Therefore, this article argues that the obviousness analysis for AI-assisted inventions requires urgent reconsideration. If the standard remains unchanged, this will set a very low bar for patentability leading to an increasing number of patents. This, in turn, will exacerbate an already major problem of patent accumulation in this field that contributes to high drug prices and the unaffordability of medicines.

It is suggested in this article that the proper test for the obviousness analysis needs to take into account the advancement of AI technology, which should be adequately integrated into the assessment to provide a fair benchmark for AI-assisted inventions. To achieve this, it is suggested that AI should be incorporated into the standard of the skilled person as a tool that such a person uses to achieve the invention. Importantly, to establish an appropriate level of skills and techniques for the skilled person, such a person must be equipped with an equivalent AI that was used in the creation of the invention or the best available AI in the relevant field. The use of an equivalent AI, or a superior one, would help to concentrate the analysis on the capabilities and knowledge of the skilled person, rather than on the computational powers of AI. Once an appropriate benchmark is set, the obviousness analysis would need to consider whether it would be obvious for the skilled person to achieve such a result using AI. It is also submitted in this article that the use of AI significantly increases the level of a reasonable expectation of success and, in some cases, such an expectation can be presumed. This issue is likely to be addressed by existing mechanisms as explained above. Finally, in certain circumstances, the use of AI in the process of drug discovery may be considered a routine procedure. In the absence of some evidence demonstrating that, to arrive at the invention, the skilled person would have to overcome some problems in a non-obvious way, the results of such a routine process may be considered obvious. While the suggested approach elevates the bar for patentability of AI-assisted inventions, it, nevertheless, reflects the advancements of AI technology in the field. It is believed that the suggested approach will provide a fair balance of protection granted to the owners of patents on AI-assisted inventions and society.

References

Abbott, R. (2018). Everything Is Obvious. UCLA L. Rev., 66, 2.

Ban, T.A. (2006). The Role of Serendipity in Drug Discovery. Dialogues Clin Neurosci., 8, 335–344.

Bently, L. et al (2018). Intellectual Property (5th edn) OUP.

Bishop, C.M. (2013). Model-based machine learning. Philos. Trans. A Math. Phys. Eng. Sci., 371.

Birss, C. et al. (2020). Terrell on the Law of Patents (19th Edn.). Sweet & Maxwell.

Block, P. (2017). The inventor's new tool: artificial intelligence – how does it fit in the European patent system? European Intellectual Property Review, 39(2), 69-73.

Boulet, P. et al (2003). Drug patents under the spotlight**.** Sharing practical knowledge about pharmaceutical patents. Médecins Sans Frontières.

Buteau, K. (2010). Deuterated Drugs: Unexpectedly Nonobvious. J. High Tech. L., 10(1), 38.

Carrasco-Ramiro, F., Peiro-Pastor, R. and Aquado, B. (2017). Human genomics projects and precision medicine. Gene Therapy, 24, 551–561.

Challener C.A., (2018). Can Artificial Intelligence Take the Next Step for Drug Repositioning? Pharmaceutical Technology Europe, 14.

Chen Y. et al. (2016). IBM Watson: How Cognitive Computing Can Be Applied to Big Data Challenges in Life Sciences Research, Clinical Therapeutics, 38

CIPA. (2019). CIPA Guide to the Patents Acts (9thEdn.) Sweet & Maxwell.

VOL: 2, ISSUE: 8
August/2020
https://ijssppnet.com/
E-ISSN: 2663-7200
DOI: 10.33642/ijsspp.v2n8p2

DiMasi, J.A. et al (2016). Innovation in the pharmaceutical industry: New estimates of R&D costs. Journal of Health Economics, 47.

Duch, W. et al. (2007). Artificial intelligence approaches for rational drug design and discovery. Curr. Pharm. Des. 13, 1497–1508.

Emig, D. et al. (2013). Drug target prediction and repositioning using an integrated network-based approach. PLoS One 8, e60618

EFPIA (2018). The Pharmaceutical Industry in Figures. Key Data 2018, 2. Available at <https://efpia.eu/media/361960/efpia-pharmafigures2018_v07-hq.pdf>.

European Commission (2018). Artificial intelligence, real benefits. Available at <https://ec.europa.eu/digital-single-market/en/news/artificial-intelligence-real-benefits>.

European Commission. (2020). White Paper On Artificial Intelligence - A European approach to excellence and trust, 2. Available at <https://ec.europa.eu/info/sites/info/files/commission-white-paper-artificial-intelligence-feb2020_en.pdf>.

Fabris, D. (2020). From The Phosita To The Mosita - Will "Secondary Considerations" Save Pharmaceutical Patents From Artificial Intelligence? IIC, 52.

Finnie, P.J. (2018). AI-generated in silico data in patent applications. Drug Discovery Today, 23(10), 1693.

Fleming, N. (2018). How artificial intelligence is changing drug discovery. Nature. Available at <https://www.nature.com/articles/d41586-018-05267-x>.

Fleming, N. (2018). Computer-calculated compounds. Researchers are deploying artificial intelligence to discover drugs. Nature, 557, S55.

Fraser, E. (2016). Computers as inventors – legal and policy implications of artificial intelligence on patent law. SCRIPTed, 13(3), 305-333.

Grubb, P.W. et al. (2016). Patents for Chemicals, Pharmaceuticals, and Biotechnology. Fundamentals of Global Law, Practice and Strategy (6th edn) OUP.

Gurgula, O. (2017). Strategic Accumulation of Patents in the Pharmaceutical Industry and Patent Thickets in Complex Technologies – Two Different Concepts Sharing Similar Features. IIC, 48(4).

Hargrave, T.E., Bo, Y., & Johannes, R. (2012). Serendipity in Anticancer Drug Discovery. World J Clin Oncol, 3, 1–6.

Hattenbach, B. & Glucoft, J. (2015). Patents in an era of infinite monkeys and artificial intelligence. Stanford Technology Law Review, 19, 32-51.

Hughes, J.P. et al. (2011). Principles of early drug discovery. Br. J. Pharmacol. 162, 1239–1249.

Iglesias, M., Shamuilia, S., & Anderberg, A. (2019). Intellectual Property and Artificial Intelligence: A literature Review. European Commission, 13.

Ismail K. & John L. (2004). Can the Pharmaceutical Industry Reduce Attrition Rates? Nat Rev Drug Discov, 3:711.

Kashoki M. et al. (2020). A Comparison of EMA and FDA Decisions for New Drug Marketing Applications 2014–2016: Concordance, Discordance, and Why. Clinical Pharmacology & Therapeutics, 107: 1

Klopman, G. et al. (2004). ESP: a method to predict toxicity and pharmacological properties of chemicals using multiple MCASE databases. J. Chem. Inf. Comput. Sci. 44, 704–715.

Lee, J.-G. et al. (2017). Deep learning in medical imaging: general overview. Korean J. Radiol., 18, 570–584.

Lemley, M.A. (2017). Expecting the Unexpected. Notre Dame L. Rev., 92.

Lohr, S. (2013). And now, from I.B.M., Chef Watson. New York Times. Available at <http://www.nytimes.com/2013/02/28/technology/ibm-exp loring-new-feats-for-watson.html?_r=0>.

VOL: 2, ISSUE: 8
August/2020
https://ijssppnet.com/
E-ISSN: 2663-7200
DOI: 10.33642/ijsspp.v2n8p2

Mak K.K & Pichika M.R. (2019). Artificial intelligence in drug development: present status and future prospects. Drug Discovery Today, 24(3), 775.

Menden, M.P. et al. (2013). Machine learning prediction of cancer cell sensitivity to drugs based on genomic and chemical properties. PLoS One 8, e61318.

Merk, D. et al. (2018). De novo design of bioactive small molecules by artificial intelligence. Mol. Inform. 37, 1700153.

Mullard A. (2017). The drugmaker's guide to the galaxy. Nature, 549, 445–447.

Nascimento, A.C.A. et al. (2016). A multiple kernel learning algorithm for drugtarget interaction prediction. BMC Bioinf. 17, 46.

Osterloh, I.H. (2004). The discovery and development of Viagra ® (sildenafil citrate). In U. Dunzendorter (Ed.), Sildenafil (pp. 1-13). Birkhauser Verlag/Switzerland.

Paul, S. M. et al. (2010). How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nature Rev. Drug Discov. 9, 203–214.

Ramalho, A. (2018). Patentability of AI-Generated Inventions: Is a Reform of the Patent System Needed? Available at <https://ssrn.com/abstract=3168703>.

Reinbold, P. (2020). Taking Artificial Intelligence Beyond the Turing Test. Wisconsin Law Review, 2020

Riccardo B. (2014). Big Data and Biomedical Informatics: A Challenging Opportunity. IMIA Yearbook of Med Inf., 8–13.

Sacks LV., et al. (2014). Scientific and Regulatory Reasons for Delay and Denial of FDA Approval of Initial Applications for new Drugs 2000-2012. JAMA, 378–384.

Seddon, G. et al. (2012). Drug design for ever, from hype to hope. J. Comput. Aided Mol. Des. 26, 137–150.

Simon, B.M. (2013). The implications of technological advancement for obviousness. Michigan Telecommunications and Technology Law Review, 19.

Sir Hugh Laddie (2004). Patents-what's invention got to do with it? In D. Vaver & L. Bently (Eds.), Intellectual Property in the New Millennium, 91-93, CUP.

Shemtov, N. (EPO, 2019). A study on inventorship in inventions involving AI activity.

Shlomit Y.-R., & Liu, X. (2017). When Artificial Intelligence Systems Produce Inventions: The 3A Era and an Alternative Model for Patent Law. Cardozo Law Review, 39, 2215-2263. Available at <https://ssrn.com/abstract=2931828>.

Smith, S. (2018). 6 Things We Learned about Artificial Intelligence in Drug Discovery from 330 Scientists. Available at <https://blog.benchsci.com/6-things-we-learned-about-artificial-intelligence-in-drug-discovery-from-330-scientists>.

Smith, S. (2020). 230 Startups Using Artificial Intelligence in Drug Discovery. Available at <https://blog.benchsci.com/startups-using-artificial-intelligence-in-drug-discovery>.

Sullivan, C. & Kline, M. (2016). Introduction to Patentability in Drug Development. Future Science Ltd., 90.

Swartz, A. (2018). Drug discoveries rely less on luck and more on tech. The Washington Post. 05/14/2018.

Tafuri G. et al, (2013). Disclosure of grounds of European withdrawn and refused applications: a step forward on regulatory transparency. Br J Clin Pharmacol, 75(4), 1149–1151.

Trask, A.V. (2008). Obvious to Try: A Proper Patentability Standard in the Pharmaceutical Arts. Fordham L. Rev., 76(5).

VOL: 2, ISSUE: 8
August/2020
https://ijssppnet.com/
E-ISSN: 2663-7200
DOI: 10.33642/ijsspp.v2n8p2

UNCTAD (2015). The role of competition in the pharmaceutical sector and its benefits for consumers. TD/RBP/CONF.8/3, 3.

Vertinsky, L. (2018). Thinking Machines and Patent Law. In W. Barfield & U. Pagallo (Eds.). Research Handbook of Artificial Intelligence (Edward Elgar Publishing).

Viola, R. (2019). Finding the cures for cancer: AI and supercomputers paving the way to personalised medicine. Available at <https://ec.europa.eu/digital-single-market/en/blogposts/finding-cures-cancer-ai-and-supercomputers-paving-way-personalised-medicine>'

VoPham, T. et al. (2018). Emerging trends in geospatial artificial intelligence (geoAI): potential applications for environmental epidemiology. Environ. Health, 17, 40

34

Wolff, M.E. (2011). Drug discovery market exclusivity after KSR: The challenge to pharmaceutical scientists and the US congress. Journal of Pharmaceutical Sciences, 100(8).

Workman P., Antolin A.A. & Al-Lazikani B. (2019). Transforming cancer drug discovery with Big Data and AI. Drug Discovery, 14:11, 1091.

Yanisky-Ravid, S. & Liu, X. (2017). When Artificial Intelligence Systems Produce Inventions: The 3A Era and an Alternative Model for Patent Law. Cardozo Law Review, Forthcoming. Available at <https://ssrn.com/abstract=2931828>.

Zeng et al. (2020). Target identification among known drugs by deep learning from heterogeneous networks. Chem. Sci., 11, 1775.