THIS VERSION DOES NOT CONTAIN PAGE NUMBERS.
PLEASE CONSULT THE PRINT OR ONLINE DATABASE
VERSIONS FOR THE PROPER CITATION INFORMATION.

ARTICLE

DESCRIBING BLACK-BOX MEDICINE

W. NICHOLSON PRICE II[1]

INTRODUCTION

Personalized medicine is a touchstone of modern medical science, and is increasingly addressed in the legal literature.[2] In personalized medicine, treatments are chosen and tailored based on the characteristics of the individual patient.[3] However, personalized medicine today is largely limited to those relatively simple relationships that can be explicitly characterized and validated through the scientific process and through clinical trials.[4]

A new type of personalized medicine, which I call "black-box medicine," seeks to expand the reach of personalized medicine, and medical science in general, by leveraging implicit, complex relationships beyond the reach of

---

[1] Assistant Professor of Law, University of New Hampshire School of Law. I wish to thank Ana Bracic, Michael Meurer, Rachel Sachs, and the participants at the Boston University Workshop on Personalized Medicine and Intellectual Property for helpful feedback on an earlier version of this paper. All errors are my own.

[2] Personalized medicine is relatively new to the legal literature, but is increasingly addressed. In addition to the works in this volume, see, e.g., Barbara J. Evans, *What Will It Take to Reap the Clinical Benefits of Pharmacogenomics?*, 61 FOOD & DRUG L.J. 753 (2006) (discussing pharmacogenomics, a subset of personalized medicine); Robin Feldman, *Whose Body Is It Anyway? Human Cells and the Strange Effects of Property and Intellectual Property Law*, 63 STAN. L. REV. 1377, 1391–92 (2011) (discussing intellectual property of personalized medicine); W. Nicholson Price II, *Unblocked Future: Why Gene Patents Won't Hinder Whole Genome Sequencing and Personalized Medicine*, 33 CARDOZO L. REV. 1601 (2012) (discussing gene patents and personalized medicine). Personalized medicine has also received extensive attention in the medical literature. *See, e.g.*, Wylie Burke & Bruce M. Psaty, *Personalized Medicine in the Era of Genomics*, 298 J. AM. MED. ASS'N 1682 (2007); Isaac S. Chan & Geoffrey S. Ginsburg, *Personalized Medicine: Progress and Promise*, 12 ANN. REV. GENOMICS & HUM. GENETICS 217 (2011); Geoffrey S. Ginsburg & Jeanette J. McCarthy, *Personalized Medicine: Revolutionizing Drug Discovery and Patient Care*, 19 TRENDS BIOTECH. 491 (2001); Margaret A. Hamburg & Francis S. Collins, *The Path to Personalized Medicine*, 363 NEW ENG. J. MED. 301 (2010).

[3] PRESIDENT'S COUNCIL OF ADVISORS ON SCI. & TECH., PRIORITIES FOR PERSONALIZED MEDICINE 1 (2008).

[4] *See, e.g.*, Chan & Ginsburg, *supra* note 2, at 225 (listing molecular diagnostics for personalized disease classification and treatment).

THIS VERSION DOES NOT CONTAIN PAGE NUMBERS.
PLEASE CONSULT THE PRINT OR ONLINE DATABASE
VERSIONS FOR THE PROPER CITATION INFORMATION.

current analytical science.[5] Black-box medicine uses nontransparent algorithms to find patterns hidden in the wealth of individual health care data being generated and collected today.[6] This approach promises a faster, less expensive path to leverage many novel biological relationships, increasing possibilities for treatment decisions and developing new therapeutics.[7] Accordingly, I define black-box medicine as "the use of opaque computational models to make decisions related to health care."[8]

Black-box medicine has great promise, but also raises significant issues and concerns, especially regarding the incentives available for its development.[9] In terms of patent incentives, whether black-box medicine comprises patentable subject matter is a distinct concern, but one that is difficult to answer precisely in a time of changing doctrine.[10] But patents for black-box medicine may fall to a more prosaic challenge: the disclosure requirement of 35 U.S.C. § 112, in particular the enablement and written description requirements. This brief Article addresses this issue and concludes that although disclosure is a major hurdle for the patentability of black-box medicine, it is not an insurmountable problem.

---

[5] For a more detailed description of black-box medicine and a summary of legal issues it raises, *see* W. Nicholson Price II, *Black-Box Medicine*, 28 HARV. J.L. & TECH. 419 (2015).

[6] *Id.* at 429–34.

[7] *Id.* at 434–37.

[8] *Id.* at 421.

[9] Black-box medicine raises other questions in many arenas, including regulation, commercialization, privacy, and other issues of intellectual property and incentives; those questions demand significant further study. For an initial discussion of these issues, *see id.* at 442–66.

[10] The Supreme Court's recent decisions on patentable subject matter leave the patentability of pure algorithms, even those with substantial medical effects, in substantial doubt. *See* Alice Corp. v. CLS Bank Int'l, 134 S. Ct. 2347, 2358, 2360 (2014) (holding that mere addition of a general-purpose computer or storage media is insufficient to make an otherwise unpatentable algorithm patentable); Mayo Collaborative Servs. v. Prometheus Labs., Inc., 132 S. Ct. 1289, 1294-95 (2012) (finding unpatentable a simple explicit personalized medicine algorithm for determining drug dosage by measuring metabolite levels and comparing those to predetermined thresholds). In *Alice*, the Supreme Court held that if the essence of an invention is unpatentable subject matter, the court must then determine whether "'the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.'" *Alice*, 134 S. Ct. at 2355 (quoting *Mayo*, 132 S. Ct. at 1294) (alteration in original). A full exploration of whether and which black-box medicine implementations comprise patentable subject matter is ongoing and outside the scope of this work. For an exploration of the effect of the Supreme Court's gene patent decision in *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013), on personalized medicine, see Stephanie S. Lim, Note, *Gene Patents in the Wake of Association for Molecular Pathology v. Myriad Genetics, Inc.: An International Perspective on Pharmacogenomics*, 23 CARDOZO J. INT'L & COMP. L. 99 (2014).

THIS VERSION DOES NOT CONTAIN PAGE NUMBERS.
PLEASE CONSULT THE PRINT OR ONLINE DATABASE
VERSIONS FOR THE PROPER CITATION INFORMATION.

This Article proceeds in two parts. Part I describes the concept of black-box medicine in more detail, describing briefly the baseline of extant personalized medicine and then addressing how black-box medicine departs from that baseline. Part II turns to the questions of enablement and written description as a requirement for obtaining a patent, briefly summarizing the doctrine and then applying it to black-box medicine. A few final thoughts conclude.

BLACK-BOX MEDICINE

Black-box medicine is a developing concept in the fields of medicine, science, and law. In a nutshell, black-box medicine greatly extends the reach of personalized medicine to make predictions and treatment recommendations by leveraging complex, implicit biological relationships gleaned from algorithmic exploration of large health datasets.[11] That characterization requires quite a bit of unpacking. This section briefly defines personalized medicine, then explains black-box medicine and describes how it differs from personalized medicine as currently understood.

Personalized medicine typically refers to the notion that treatment should be tailored to take account of differences between patients.[12] In one sense, this is a tautological description of medical care, since medical care involves individual interactions between doctors and the specific patients they are treating; most doctors presumably would describe their treatment as "personalized." However, personalized medicine as used in this context refers more specifically to the use of relationships between specific biological traits of a patient—for instance, whether a patient produces the version of an enzyme that will metabolize and inactivate a drug quickly or slowly—to make decisions about treatment—for instance, what dose of the drug to give the patient.[13] Typically, such relationships are discovered in medical practice or in a laboratory, carefully studied, and then verified in the course of clinical trials before entering into practice.[14] Because of the difficulties in demonstrating

[11] Price, *supra* note 5, at 429–34.

[12] *See* PRESIDENT'S COUNCIL OF ADVISORS ON SCI. & TECH., *supra* note 3, at 1.

[13] *Id.* (personalized medicine can "classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment."). For a specific example of matching drug dosage to individual characteristics, see Chan & Ginsburg, *supra* note 2, at 227 (discussing the use of genetic testing for two genes, combined with clinical variables such as height, weight, and sex, to determine appropriate doses for the blood-thinning drug warfarin).

[14] *See, e.g.*, FDA, GUIDANCE FOR INDUSTRY: CLINICAL PHARMACOGENOMICS: PREMARKET EVALUATION IN EARLY-PHASE CLINICAL STUDIES AND RECOMMENDATIONS FOR LABELING 6-7 (2013), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM337169.pdf, (archived at http://perma.cc/RNF4-JTSQ) (providing guidance for industry on the use and development of genetic information in drug trials).

THIS VERSION DOES NOT CONTAIN PAGE NUMBERS.
PLEASE CONSULT THE PRINT OR ONLINE DATABASE
VERSIONS FOR THE PROPER CITATION INFORMATION.

causation in both basic and clinical scientific research, this form of personalized medicine, which I call "explicit personalized medicine," is limited to relatively simple biological relationships, where at most a few patient variables are involved.[15]

Evaluating more complex relationships strains the statistical power of experiments, demanding extremely large clinical trials at prohibitive expense.[16] Unfortunately, given the reality that many biological relationships are extremely complex,[17] explicit personalized medicine must leave untapped a large swath of biological variation.

Black-box medicine seeks to resolve this challenge by removing the "explicit" element from personalized medicine by using relationships without fully understanding them or even clearly identifying them. Data about the health of individuals is being generated at prodigious rates, whether as the result of genetic sequencing,[18] metabolic screens,[19] or straightforward traditional diagnostic tests and medical charts, especially if they are are entered into electronic health records.[20] Buried in this data are the relationships that reflect underlying biological linkages.[21] While these relationships may now be—and may long remain—outside the reach of explicit scientific research, they are increasingly accessible to sophisticated nontransparent data mining techniques, known as "machine learning."[22] A key feature of such techniques

---

[15] *See* Price, *supra* note 5, at 427–29.

[16] *Cf.* Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 TEX. L. REV 503, 510–11 (2008) (noting the half-billion dollar costs of pharmaceutical clinical trials).

[17] *See, e.g.*, Hojin Moon et al., *Ensemble Methods for Classification of Patients for Personalized Medicine with High-Dimensional Data*, 41 ARTIFICIAL INTELLIGENCE MED. 197, 198, 203–04 (2007) (using 5,000 genes to classify lung tumors).

[18] Genetic sequencing for individual variants is becoming cheap and common, and whole-genome sequencing is rapidly dropping in price. Erika Check Hayden, *Is the $1,000 Genome for Real?*, NATURE NEWS: EXPLAINER (Jan. 15, 2014), *available at* http://www.nature.com/news/is-the-1-000-genome-for-real-1.14530 (archived at http://perma.cc/2XAM-RGLV); Radoje Drmanac, *The Advent of Personal Genome Sequencing*, 13 GENETICS MED. 188, 188 (2011), *available at* http://www.nature.com/gim/journal/v13/n3/full/gim9201135a.html (archived at http://perma.cc/9R5M-SZYP).

[19] Chan & Ginsburg, *supra* note 2, at 222–24.

[20] Although the adoption of electronic health records has been slower than expected, new incentives promise to accelerate their spread. Ashish K. Jha et al., *A Progress Report On Electronic Health Records In U.S. Hospitals*, 29 HEALTH AFF. 1951, 1951-53, 1957 (2010) (finding an increase in U.S. hospitals using electronic health records from 8.7% in 2008 to 11.9% in 2009).

[21] *See, e.g.*, Moon et al., *supra* note 17, at 198, 203–04 (using data from about 5,000 genes to accurately sort two types of lung tumors responsive to different therapies).

[22] The machine-learning literature is extensive and highly technical. For a brief sample,

THIS VERSION DOES NOT CONTAIN PAGE NUMBERS.
PLEASE CONSULT THE PRINT OR ONLINE DATABASE
VERSIONS FOR THE PROPER CITATION INFORMATION.

is that they improve groupings and predictions within a set of data over many computational iterations; eventually, the approach converges on a result, which is returned.[23] Predictions for a new observation—say, a new patient—can then be made based on how the new observation's characteristics fit into the patterns found in the larger initial dataset.[24]

A tremendously simplified example of this type of approach is seen in the recommendation systems used by companies, like Netflix, to recommend videos or other products.[25] Assume that Netflix's prediction algorithm determines that, among its millions of movie ratings, individuals who rate highly both *Star Trek: The Next Generation* and *The Princess Bride* also tend to enjoy Fred Astaire's dancing films. Presented with a new customer who enjoys *Star Trek* and *The Princess Bride*, Netflix can recommend that the customer try Fred Astaire's films without any idea what constellation of taste ties all the preferences together. Similarly, if a parallel approach in the health care environment reveals that young women with specific combinations of a dozen genes who live in urban environments are much more likely to develop very aggressive breast cancer, asymptomatic women with those characteristics could be targeted by frequent mammograms despite falling outside standard guidelines—again, even though we might have no idea what the genes do or what urban environmental factor might be involved. This opacity is what makes black-box medicine "black-box."

The nontransparency of black-box medicine exists at two potential levels, depending on the contours of the approach used. First, the prediction may literally be fully opaque—that is, under some methodologies, though the learning process itself is known, the computational learning process leaves the learned relationships hidden.[26] The user enters inputs and receives outputs, but

see for example, CHRISTOPHER M. BISHOP, PATTERN RECOGNITION AND MACHINE LEARNING (Michael Jordan et al. eds., 2006); PETER FLACH, MACHINE LEARNING: THE ART AND SCIENCE OF ALGORITHMS THAT MAKE SENSE OF DATA (2012); Jesse Davis et al., *Machine Learning for Personalized Medicine: Will This Drug Give Me a Heart Attack?*, PROC. INT'L CONF. MACHINE LEARNING (2008), *available at* http://www.ualberta.ca/~szepesva/ICML2008Health/Davis.pdf (archived at http://perma.cc/Z6ZY-2JYM); IAN H. WITTEN & EIBE FRANK, DATA MINING: PRACTICAL MACHINE LEARNING TOOLS AND TECHNIQUES (2d ed. 2005).

[23] *See* FLACH, *supra* note 22, at 13-19.

[24] *See* Davis et al., *supra* note 22.

[25] Netflix initially used a relatively simple prediction algorithm, Cinematch, which employed "straightforward statistical linear models with a lot of data conditioning." *Frequently Asked Questions*, NETFLIX PRIZE, http://www.netflixprize.com/faq, (last visited June 14, 2015) (archived at http://perma.cc/E7X2-HKLP). After an extensive crowdsourced competition to improve the algorithm, Netflix made slight improvements. *Id.*

[26] It may be useful to clarify between two potential meanings of algorithms; the term could meaningfully be applied either to the algorithm driving the machine learning process or to the eventual decision-making algorithm reached after the machine has "learned." I

THIS VERSION DOES NOT CONTAIN PAGE NUMBERS.
PLEASE CONSULT THE PRINT OR ONLINE DATABASE
VERSIONS FOR THE PROPER CITATION INFORMATION.

the relation between those is hidden within the "black box" of the algorithm.[27] In a human analogy, imagine the decisions of an experienced radiologist who has read many thousands of X-rays. She can look at an X-ray and correctly identify which spots on an image are tumors and which are not, but may be unable to explicitly state the algorithm she uses to make that determination; the knowledge is implicit. Some machine learning techniques are similarly opaque. For instance, a leading technique using "deep neural networks" explicitly models its learning process on using multiple "hidden layers" of simulated human neurons to classify observations based on extensive practice.[28] Although the trained neural network can accurately classify images or predict risk, it is difficult or impossible to extract the algorithm the network uses for classification.[29]

Second, and perhaps more comfortably, other approaches can explicitly state a relationship identified by the approach, but that relationship is so complex as to be opaque in terms of current understanding. For instance, assume that a learning algorithm processes data and returns a result that patients with thirty different characteristics within thirty different interconnected ranges of values are more likely to respond well to a particular medical treatment. While this relationship can be stated explicitly, it is almost certainly far too complex for scientists to understand the underlying biology or to validate in the context of a clinical trial, and is therefore practically nontransparent, even if not formally so. Though this distinction matters little in terms of developing science or practicing medicine, it has potential consequences for the availability of patent incentives.[30]

This inability to verify relationships through clinical trials is both a strength and a weakness of black-box medicine. On the one hand, clinical trials and scientific understanding provide our primary information that a particular relationship is real; without them, black-box medicine must rely on other forms

focus here on the latter—that is, the underlying biological relationships and the algorithms which track those relationships, not the algorithms which dictate the contours of the machine learning process. For a general description of algorithms in machine learning, *see* FLACH, *supra* note 22.

[27] *Id.*

[28] *See, e.g.*, Turgay Ayer et al., *Breast Cancer Risk Estimation with Artificial Neural Networks Revisited: Discrimination and Calibration*, 116 CANCER 3310, 3312-13, 3316 (2010) (describing use of an artificial neural network with 1,000 hidden layer nodes of simulated neurons to classify risk of breast cancer in a dataset of 62,219 mammography findings; the trained network performed better than trained radiologists).

[29] *See, e.g.*, Eleni Orphanidou-Vlachou et al., *Texture Analysis of T_1- and T_2-Weighted MR Images and Use of Probabilistic Neural Network to Discriminate Posterior Fossa Tumours in Children*, 27 NMR BIOMED. 632, 633, 637 (2014) (finding a neural network approach superior to a more explicit approach in identifying brain tumors in children); Ayer et al., *supra* note 28, at 3316.

[30] *See infra* Part II.

THIS VERSION DOES NOT CONTAIN PAGE NUMBERS.
PLEASE CONSULT THE PRINT OR ONLINE DATABASE
VERSIONS FOR THE PROPER CITATION INFORMATION.

of validation, based in observational data rather than clinical experiment.[31] On the other hand, clinical trials are incredibly expensive and time-consuming.[32] Black-box medicine provides the ability to develop medical options, including previously unavailable complex implicit biological relationships, without incurring that cost or delay.[33]

In addition to efficiency gains, black-box medicine may have substantial practical benefits in the guidance of new treatment options and the development of drugs. Existing treatments, whether pharmaceutical or otherwise, can be guided by the relationships found by black-box algorithms.[34] In addition, black-box medicine enhances the possibility of identifying new uses for approved drugs.[35] Overall, black-box medicine promises substantial additions to the toolbox of medical development and medical treatment.

While black-box medicine opens major new opportunities for medicine, its path forward is far from smooth. A full accounting of the challenges ahead is beyond the scope of this work,[36] but this Article attempts to tackle at least one potential concern: the potential bar of the written description and enablement requirements to patent incentives for development.

SECTION 112 AND PATENT INCENTIVES

Black-box medicine requires significant resources to develop; datasets must

[31] *See* Price, *supra* note 5, at 440–42.

[32] *See*, *e.g.*, Joseph A. DiMasi et al., The Price of Innovation: New Estimates of Drug Development Costs, 22 J. HEALTH ECON. 151, 165 (2003) (estimating clinical-trial costs of $467 million).

[33] Taken farther in this direction, black-box medicine's central lack of transparency is amplified by the eventual potential for dynamic models. If predictive models are based on large datasets, and if those models are improved by the availability of larger amounts of data, models can change and be improved dynamically as the datasets grow. *See* Price, *supra* note 5, at 460. This possibility makes the validation of models—and their regulation—dramatically more challenging, since the model becomes a moving target. *Id*. Since dynamic models are an even more radical departure from current medical practice, and are some way further off, this Article does not address them separately.

[34] For instance, real-time treatment decisions about which patients would benefit most from access to an intensive care unit, which patients would benefit most from an organ transplant, or which patients can most safely be discharged, can all be made via black-box algorithms. I. Glenn Cohen et al., *The Legal and Ethical Concerns That Arise from Using Complex Predictive Analytics in Health Care*, 33 HEALTH AFF. 1139, 1139-40, 1146 (2014).

[35] Most drugs have multiple medically useful effects, but drug companies have only weak incentives to conduct clinical trials for later uses of an approved drug, since patent protection on those uses is weak and off-label use is both legal and common. *See* Rebecca S. Eisenberg, *The Problem of New Uses*, 5 YALE J. HEALTH POL'Y L. & ETHICS 717, 725–28 (2005); Benjamin N. Roin, Solving the Problem of New Uses 2-4, 30-31 (Oct. 1, 2013) (unpublished manuscript) (on file with Harvard DASH).

[36] For a brief introduction to some potential problems, *see* Price, *supra* note 5.

THIS VERSION DOES NOT CONTAIN PAGE NUMBERS.
PLEASE CONSULT THE PRINT OR ONLINE DATABASE
VERSIONS FOR THE PROPER CITATION INFORMATION.

be gathered and curated, algorithms must be developed, and suggestions must be validated to the extent possible.[37] Patents serve as protection and, at least potentially, a primary incentive for this kind of costly information good.[38] But for patent exclusivity to be available, the invention must meet a set of statutory requirements.[39] One key hurdle, the patentable subject matter bar of § 101, is the subject of evolving law and academic discussion.[40] However, another, more prosaic requirement is also involved: the patent must include an enabling written description of the invention.[41] This section addresses the difficulties for black-box medicine in meeting this requirement.

Under 35 U.S.C. § 112, a patent "shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art . . . to make and use the same . . . ."[42] This section includes both a requirement that the invention be adequately described ("written description") and that the patent specification enable others to practice the invention ("enablement");[43] "[a]lthough there is often significant overlap between [these requirements], they are nonetheless independent of each other."[44]

When addressing these requirements, the difference between formal and

---

[37] *Id.* at 437–42.

[38] *See, e.g.*, Mark A. Lemley, *Ex Ante versus Ex Post Justifications for Intellectual Property*, 71 U. CHI. L. REV. 129, 129-33 (2004). Patents may not be the ideal source of incentives for health information of this sort, not least because of challenges excluding others, which decreases incentives and may result in socially suboptimal incentives even if patents are available. *See* Amy Kapczynski & Talha Syed, *The Continuum of Excludability and the Limits of Patents*, 122 YALE L.J., 1900, 1905–16 (2013). Other incentives are also available, such as prizes, grants, tax incentives, and regulatory exclusivity, but will not be discussed here. *See, e.g.*, Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 346-52 (2007) (discussing regulatory exclusivity); Daniel J. Hemel & Lisa Larrimore Ouellette, *Beyond the Patents–Prizes Debate*, 92 TEX. L. REV. 303 (2013) (discussing the theoretical equivalence of different forms of incentives).

[39] 35 U.S.C. §§ 101 (patentable subject matter, utility), 102 (novelty), 103 (nonobviousness), and 112 (written description, enablement, and best mode) (2012).

[40] *Id.* § 101. For academic discussion, see, among many others, Rebecca S. Eisenberg, *Prometheus Rebound: Diagnostics, Nature, and Mathematical Algorithms*, 122 YALE L.J. ONLINE 341 (2013); Mark A. Lemley et al., *Life After Bilski*, 63 STAN. L. REV 1315 (2011). *See also supra* note 10 (listing recent Supreme Court § 101 cases).

[41] 35 U.S.C. § 112.

[42] *Id.* §112(a). Section 112 also requires that the patent applicant disclose the best mode of practicing the invention, *id*, but under the America Invents Act, failing to meet this requirement is no longer grounds for invalidating a patent. *Id.* § 282. Accordingly, this toothless requirement will not be addressed here.

[43] *Id.* § 112(a).

[44] Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 921 (Fed. Cir. 2004).

THIS VERSION DOES NOT CONTAIN PAGE NUMBERS.
PLEASE CONSULT THE PRINT OR ONLINE DATABASE
VERSIONS FOR THE PROPER CITATION INFORMATION.

practical nontransparency described above abruptly gains traction.[45] If a process is only practically nontransparent—that is, if the data-crunching yields a formula of the form "if these 30 variables are within specified ranges, then do X; otherwise do Y"—written description is possible, even if that description provides little scientific understanding and if the inventor herself lacks such understanding.[46] Similarly, a person of ordinary skill in the art can practice the invention by applying the formula, even without knowing why the resulting recommendation is useful or why the formula works; accordingly, the invention can meet the enablement requirement. However, claims must be commensurate with the scope of disclosure, and disclosure of a very specific formula without understanding which aspects can be broadened will be unlikely to support the grant of broad claims; accordingly, the protected subject matter may be quite narrow.[47]

If, on the other hand, a process is formally and fully nontransparent—that is, it remains locked within the "black box" that gives recommendations when provided with input variables—then explicitly describing the full process becomes an impossibility. Similarly, others cannot be enabled to use the invention by information contained within the patent specification, because no such adequate information can be provided.

In such a case, meeting the written description requirement may be possible, but would likely require creative efforts. One possibility would be a modified form of the deposit currently allowed for self-replicating biological entities; a copy of the entire algorithm could be deposited in a publically accessible repository rather than attempting to describe the algorithm in the patent document.[48]

---

[45] *See supra* Part I.

[46] An inventor need not understand what she has invented to receive a patent; indeed, nor need anyone else. Diamond Rubber Co. of New York v. Consol. Rubber Tire Co., 220 U.S. 428, 435–36 (1911).

[47] *See* Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc., 166 F.3d 1190, 1196 (Fed. Cir. 1999) ("The scope of the claims must be less than or equal to the scope of the enablement. The scope of enablement, in turn, is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation.").

[48] *See* Enzo Biochem, Inc. v. Gen-Probe, Inc., 323 F.3d 956, 965 (Fed. Cir. 2002) ("[R]eference in the specification to a deposit may also satisfy the written description requirement with respect to a claimed material."); *see also* U.S.P.T.O., MANUAL OF PATENT EXAMINING PROCEDURE § 2402 (9th ed. 2014) ("Where the invention involves a biological material and words alone cannot sufficiently describe how to make and use the invention in a reproducible manner, access to the biological material may be necessary for the satisfaction of the statutory requirements for patentability under 35 U.S.C. § 112."). It is unclear whether an algorithm developed using a stochastic machine-learning process—that is, where using the same data and same process might result in a slightly different outcome—would fall prey to written description concerns if the components were deposited.

THIS VERSION DOES NOT CONTAIN PAGE NUMBERS.
PLEASE CONSULT THE PRINT OR ONLINE DATABASE
VERSIONS FOR THE PROPER CITATION INFORMATION.

Another possibility—also drawing from the realm of hard-to-describe biological inventions—would be to rely on product-by-process claims, disclosing the process for creating the algorithm, along with the dataset involved, and claiming the algorithm created by that process.[49] However, product-by-process claims are especially difficult to enforce, since they do not cover the same result if reached by different means.

Overall, black-box medicine seems likely to encounter significant difficulties meeting the disclosure requirements of § 112.[50] Both written description and enablement are challenging bars when the invention itself has an inextricable element of opacity. Workaround techniques such as deposition or product-by-process claims may allow claims for formally nontransparent implementations of black-box medicine, though they might not be necessary for practically nontransparent algorithms that can at least be written down. The appropriate balance between those two forms of black-box medicine depend to some extent on technological advances, but also on the relative incentives available to each; differences in patentability might then be expected to shift that balance. But for any form, granted claims are likely to be quite narrow, and are thus likely to provide relatively small incentives for the development of black-box medicine in the first place.

CONCLUSION

Black-box medicine promises to be an important extension of personalized medicine, allowing the use of otherwise inaccessible types of biological relationships. However, it fits poorly with at least some aspects of patent law, which dampens the prospect of patent incentives for black-box medicine. Many forms of personalized medicine may be vulnerable to challenges with respect to patentable subject matter, but black-box medicine faces additional hurdles in meeting the written description and enablement requirements of § 112. Policy interventions aimed at the former problems may well leave the latter issues untouched. A better answer, and one which demands further study, may be that black-box medicine—and other forms of personalized medicine with similar characteristics—demands more active and directed incentives than those provided by the patent system.

---

[49] *See* Dmitry Karshtedt, *Limits on Hard-to-Reproduce Inventions: Process Elements and Biotechnology's Compliance with the Enablement Requirement*, 3 HASTINGS SCI. & TECH. L.J. 109, 120-22, 127-28 (2011).

[50] This ultimate conclusion admittedly depends at least somewhat on an assumption that black-box medicine will be treated by the courts as more like a biotechnology/diagnostic invention than a software invention; the latter have tended to face effectively different applications of the § 112 bars. *See, e.g.*, Dan L. Burk & Mark A. Lemley, *Is Patent Law Technology-Specific?*, 17 BERKELEY TECH. L.J. 1155, 1173-78, 1181-82 (2002); Ajeet P. Pai, Note, *The Low Written Description Bar for Software Inventions*, 94 VA. L. REV. 457, 460, 478-87 (2008).

THIS VERSION DOES NOT CONTAIN PAGE NUMBERS.
PLEASE CONSULT THE PRINT OR ONLINE DATABASE
VERSIONS FOR THE PROPER CITATION INFORMATION.