2018

Exploring Precision FDA, an Online Platform for Crowdsourcing Genomics

Jordan Paradise
Loyola University Chicago, School of Law, jparadise@luc.edu

EXPLORING PRECISION FDA, AN ONLINE PLATFORM FOR CROWDSOURCING GENOMICS

Jordan Paradise*

ABSTRACT: The U.S. Food and Drug Administration has created an online platform for the next generation sequencing community, enabling users to evaluate biomarker information and share resources. This article examines this online platform and offers several observations about potential legal and regulatory implications.

CITATION: Jordan Paradise, *Exploring PrecisionFDA, an Online Platform for Crowdsourcing Genomics*, 58 JURIMETRICS J. 267–282 (2018).

Precision medicine is here, with rapid advancements in the technologies, tools, and life-saving products entering the market for the treatment of serious and life-threatening disease. In May 2017, the United States Food and Drug Administration (FDA) approved the first cancer treatment for solid tumors based on a genetic biomarker rather than the tissue of origin.[1] One month later, the agency approved a companion diagnostic panel that uses next generation sequencing (NGS) to simultaneously screen a genetic sample for 23 cancer genes, three of which have FDA-approved therapies for non-small cell lung cancer.[2]

---

*Georgia Reithal Professor of Law, Loyola University Chicago School of Law. E-mail: jparadise@luc.edu. Many thanks to Loyola University Chicago School of Law student Sarah Johnson for research assistance. This article was presented at the Arizona State University Sandra Day O'Connor College of Law, 5th Annual Governance of Emerging Technologies: Law, Policy, and Ethics conference held on May 18, 2017.

1. Merck's Keytruda (pembrolizumab) was approved for the treatment of adult and pediatric patients with unresectable or metastatic solid tumors who are identified as having the microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) biomarker. News Release, FDA, FDA Approves First Cancer Treatment for Any Solid Tumor with a Specific Genetic Feature (May 23, 2017), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm560167.htm [https://perma.cc/Z2D7-S6BF]. While the FDA has permitted the use of biomarkers in the approval of non-cancer drugs, this is the first cancer drug approval supported by the use of a biomarker. For information on the FDA's Biomarker Qualification Program and the list of qualified biomarkers, see *Biomarkers at CDER*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/BiomarkerQualificationProgram/ucm535927.htm [https://perma.cc/P5A4-MFFH] (last updated Oct. 11, 2017).

2. The medical device is the Oncomine Dx Target Test manufactured by Life Technologies Corporation. *List of Cleared or Approved Companion Diagnostic Devices (In Vitro and Imaging Tools)*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm301431.htm [https://perma.cc/TB9G-BR3E] (last updated Jan. 3, 2018).

Together, these developments represent a "seismic shift" in the field of oncology[3] and illustrate the tremendous promise for medicine facilitated by NGS. However, innovative NGS research and data-sharing models depart in significant ways from traditional research and development relationships in the life sciences, potentially raising a host of novel legal questions.

Although NGS is cheaper and easier than traditional research, it generates an overwhelming amount of genomic information. Current NGS technologies use various emerging high-throughput platforms to sequence millions of small DNA fragments in parallel rather than relying on conventional DNA sequencing methods.[4] Once sequenced, bioinformatics analyses enable the fragments to be mapped onto a reference human genome, flagging unexpected variations in DNA, often called genetic variants.[5] Today, an entire individual genome can be sequenced using NGS for about $1,000, compared to over $10 million just ten years ago.[6] As for time, what can now be done in one day took over a decade to accomplish with previous Sanger biochemistry sequencing.[7] While the immense reduction in cost and time is impressive, experts caution that the large amount of genetic variants identified using NGS "will not always be targets for a particular disease."[8] In fact, "[t]he sheer magnitude of the information that we'll find on the genetic and molecular level is going to far surpass our capacity to run clinical trials."[9] Thus, to generate robust evidence linking NGS-identified genetic variants and related biomarkers to disease, and to therapeutic efficacy and drug response, there is much work to be done.

Medical research, and cancer research specifically, has recently embraced open-source, crowdsourcing models to address and solve NGS research challenges by tapping into "the collective wisdom and resources of the scientific community."[10] One example is Asymmetrex's crowdsourcing campaign initi-

---

3. Juliet Preston, *Another Win for Precision Medicine: FDA Approves Companion Diagnostic Panel*, MEDCITY NEWS (June 23, 2017, 6:56 PM), https://medcitynews.com/2017/06/fda-approves-first-universal-companion-diagnostic/ [http://perma.cc/5FJ8-TQET].

4. Sam Behjati & Patrick S. Tarpey, *What is Next Generation Sequencing?*, 98 ARCHIVES DISEASE CHILDHOOD 236, 236 (2013); Jay Shendure & Henlee Ji, *Next-Generation DNA Sequencing*, 26 NATURE BIOTECHNOLOGY 1135, 1135 (2008).

5. Behjati & Tarpey, *supra* note 4.

6. *The Cost of Sequencing a Human Genome*, NAT'L HUM. GENOME RES. INST., https://www.genome.gov/sequencingcosts/ [https://perma.cc/HP5B-MWBR] (last updated July 6, 2016). By 2011, the cost had dropped below $10,000. *See id.*

7. Behjati & Tarpey, *supra* note 4, at 236.

8. SARAH H. BEACHY ET AL., INST. OF MED., REFINING PROCESSES FOR THE CO-DEVELOPMENT OF GENOME-BASED THERAPEUTICS AND COMPANION DIAGNOSTIC TESTS: WORKSHOP SUMMARY 17 (2014) (quoting Walter Koch, Vice President of Global Research at Roche Molecular Systems).

9. *Id.* at 15 (quoting Felix Frueh, entrepreneur-in-residence at Third Rock Ventures).

10. *Harnessing the Crowd*, 3 CANCER DISCOVERY 130, 130 (2013). For an excellent, recent overview of types of crowdsourcing and uses in biomedical research, see Julio Saez-Rodriguez et al., *Crowdsourcing Biomedical Research: Leveraging Communities as Innovation Engines*, 17 NATURE REV. GENETICS 470 (2016).

ated in April 2015, which targeted cell biologists, tissue engineers, and regenerative medicine physicians.[11] The company used social media to announce the project and ultimately share its histone variant H2A biomarker, called H2A.Z asymmetry, with qualified respondents.[12] In exchange, respondents agreed to test the new biomarker tool to identify and count stem cells and report back with findings and data points.[13] The goal was to generate the information quicker and cheaper, possibly with an eye on eventual approval and marketing of the technology.[14] At the very least, the initiative contributed to the company's patent-protected intellectual property portfolio relating to the H2A biomarker.[15]

Industry is not the only source of crowdsourcing for genomic inquiry and exploration. Academic medical institutions, research consortia, patient advocacy groups, and others are creating crowdsourcing platforms based on tools to detect, collect, and evaluate genetic and genomic information.[16] Regulators are even getting into the NGS game—the FDA launched the online portal precisionFDA in December 2015, providing "a community platform for NGS assay evaluation and regulatory science exploration."[17] Deciphering information generated and published on this crowdsourced, cloud-based site may be integral to biomarker identification, industry standard setting, clinical trial development, and, ultimately, regulatory assessment and adaptability.

The growth of NGS crowdsourcing models necessarily means widespread collaborations of academic medical centers, researchers, patients and patient advocates, private foundations, medical product innovators, and regulators. Not all of which subscribe to the same norms and expectations in the sharing economy. Emerging questions surrounding the expansion of players facilitated by NGS crowdsourcing involve identification and management of complex conflicts of interest, proper incentive structures, access to and sharing of research samples and health information, inventorship status and patent rights, payments and contractual agreements, licensing terms, and eventual profit share. This article contributes to the conversation by exploring the precisionFDA online crowdsourcing platform in terms of use, functionality, and legal disclaimers and terms. It then offers several modest reflections on the legal and regulatory implications

---

11. The crowdsourcing platform and materials remains available to users on the web. *See Asymmetrex Crowdsourcing Evaluation of H2A.Z Asymmetry as a Universal Tissue Stem Cell Biomarker*, ASYMMETREX, https://2c94cd.campgn5.com/Asymmetrex-H2AZ-Asymmetry-Crowdsourcing-Campaign [https://perma.cc/5CAW-XC4A].

12. *See* News Release, Asymmetrex, Asymmetrex's Crowdsourcing Campaign for Evaluating a First Biomarker for Counting Adult Tissue Stem Cells Is Gaining Momentum (June 25, 2015), http://asymmetrex.com/tag/stem-cell-research/page/4/ [https://perma.cc/7XU2-LKUA].

13. *Id.*

14. *See id.*

15. Detecting and Counting Tissue-Specific Stem Cells & Uses Thereof, U.S. Pat. No. 9,081,008 (issued July 14, 2015); News Release, Asymmetrex, USPTO Issues Patent to Asymmetrex for Technologies for Counting Adult Tissue Stem Cells for the First Time (July 14, 2015), http://asymmetrex.com/tag/stem-cell-research/page/4/ [https://perma.cc/7XU2-LKUA].

16. *See, e.g.*, Saez-Rodriguez et al., *supra* note 10, at 472–73.

17. FDA, *Introduction*, PRECISIONFDA, https://precision.fda.gov/docs/intro [http://perma.cc/V3ME-WX5B].

that may arise as crowdsourcing models are integrated into research and development.

I. BRIEF HISTORY OF CROWDSOURCING

A. Early Uses and Current Scope

The concept of pooling information and resources to solve a problem is not a groundbreaking one. Scholars routinely reference the origin of the concept as 1714, the year the British government established a prize as a mechanism to gather solutions from the broad population for determining accurate longitude at sea.[18] The term *crowdsourcing* itself, however, was introduced into the lexicon in 2006.[19] *Wired Magazine* author Jeff Howe described crowdsourcing in a blog post as "the act of taking a job traditionally performed by a designated agent (usually an employee) and outsourcing it to an undefined, generally large group of people in the form of an open call."[20] The literature identifies four general categories of crowdsourcing: crowd creation (e.g., the 1714 Longitude Prize), crowd voting, crowd funding, and crowd wisdom.[21] The latter, crowd wisdom, is of relevance to the topic of crowdsourcing genomics, where the diverse knowledge base of a group is targeted to contemplate research questions.[22]

Crowd wisdom forms of crowdsourcing operate on an open source model, providing materials to users, posing a particular challenge, and aggregating the responses on a publicly available platform.[23] The open source software programs Apache and Linux are prime examples—they "involve the contribution of dispersed individuals working asynchronously to build and refine a unified product."[24] Other examples from the recent literature include crowdsourcing of digital images to populate the stock photo market,[25] crowdsourcing through municipal discussion boards to collect information about water and sewer rate

18. Jonathan J. Darrow, *Crowdsourcing Clinical Trials*, 98 MINN. L. REV. 805, 824–25 (2014); *Following the Crowd*, ECONOMIST, (Sept. 4, 2008, 12:30 PM), http://www.economist.com/node/11999251 [http://perma.cc/25J5-43FT].

19. Jeff Howe, *The Rise of Crowdsourcing*, WIRED (June 1, 2006, 12:00 PM), https://www.wired.com/2006/06/crowds/?pg=1&topic=crowds [https://perma.cc/24HP-ACVT].

20. Jeff Howe, *Crowdsourcing: A Definition*, CROWDSOURCING, http://www.crowdsourcing.com/cs/ [https://perma.cc/FRG3-GJDG] (navigate to the left side of the landing page under the author's profile photo).

21. Marc A. Lieberstein et al., *Crowdsourcing: Understanding the Risks*, INSIDE (N.Y. State Bar Ass'n., Albany, N.Y.), Fall 2012, at 34, 34.

22. *Id.* One physician in the field prefers to call crowdsourcing "knowledge media" or "knowledge networks" when social media is used to connect with patients and researchers for clinical trial input. Robert H. Carlson, *Crowdsourcing Clinical Trial Protocols*, ONCOLOGY TIMES, Mar. 25, 2014, at 30, 31.

23. *Id.*

24. Darrow, *supra* note 18, at 824.

25. *Id.* at 825.

hikes,[26] and crowdsourcing for new television commercial ideas.[27] With the explosion of social media outlets, crowdsourcing has become commonplace.

Many have reflected on the advantages and disadvantages of general crowdsourcing models and this article will not attempt to exhaust or recreate the literature on this point.[28] On the advantage side, crowdsourcing targets a large and diverse population of people, is typically not geographically limited, the rate of response is rapid and possibly ongoing, and it is less expensive than employing individuals to perform the tasks. It also energizes a community around a single goal and has the potential to generate goodwill and notoriety for the company or individual who initiated the crowdsourcing campaign. However, those responding may not necessarily be adequately qualified, there may be overwhelming rates of responses with varying utility, and there are numerous legal and ethical questions that arise, as described in Part III.

B. Crowdsourcing Medicine and Clinical Trials

In the last five years, crowdsourcing models have moved into medicine and clinical trials. Various scientific and legal commentators have traced this movement as a general matter[29] as well as the use of crowdsourcing in specific fields of medical research.[30] Others have advocated for the use of crowdsourcing to improve post-market surveillance of FDA-approved drugs.[31] While there is no one-size-fits all description of the crowdsourcing foci being undertaken in medical research and drug development, examples include clinical trial design and

---

26. *Id.*

27. *See* Lieberstein et al., *supra* note 21, at 34 (describing the Doritos "Crash the Super Bowl" campaign calling on the public to develop and submit their own commercials).

28. *See, e.g.*, *supra* notes 18–22; *infra* notes 29–35.

29. *See, e.g.*, Carlson, *supra* note 22; Patti Zettler, *Crowdsourcing Medicine?*, STAN. L. SCH.: L. & BIOSCIENCES BLOG (Apr. 23, 2015), https://law.stanford.edu/2015/04/23/lawandbiosciences-2015-04-23-crowdsourcing-medicine/ [https://perma.cc/ZD6H-CAKA].

30. *See, e.g.*, Michael Chancellor & Sarah Bartolone, *The Power of Crowdsourcing: Novel Method for Discovery of Urine Biomarkers*, 197 J. UROLOGY e399, e399 (2017); *Harnessing the Crowd*, *supra* note 10; Jonathan Lawson et al., *Crowdsourcing for Translational Research: Analysis of Biomarker Expression Using Cancer Microarrays*, 116 BRIT. J. CANCER 237, 238 (2017); Amanda Leiter et al., *Use of Crowdsourcing for Cancer Clinical Trial Development*, 106 J. NAT'L CANCER INST. 1 (2014); Matthew S. Katz, *Three Ways to Improve Clinical Trials Through Crowdsourcing*, ASCO CONNECTION (Jan. 21, 2014), https://connection.asco.org/blogs/three-ways-improve-clinical-trials-through-crowdsourcing [https://perma.cc/22EB-QP6U]; Meghana Keshavan, *Startup Crowdsourcing for Better Clinical Trials Design*, MEDCITY NEWS (Sept. 19, 2014, 11:52 AM), http://medcitynews.com/2014/09/startup-crowdsourcing-better-clinical-trial-design/.

31. Darrow, *supra* note 18, at 826; Ameet Sarpatwari et al., *Crowdsourcing Public Health Experiments: A Response to Jonathan Darrow's* Crowdsourcing Clinical Trials, 98 MINN. L. REV. 2326, 2328 (2014).

adaptation,[32] adverse event recording and interpretation,[33] biomarker identification,[34] and various other types of data collection and interpretation.[35] As early as December 2012, one life science company reported that it had received FDA clearance to pursue clinical trials for the world's first drug based on a crowdsourcing protocol, making use of telemonitoring and "remote methods for patient data collection."[36]

Recent scholarship terms crowdsourcing organized by research scientists as "challenges," which are competitions seeking voluntary labor from the scientific

---

32. *See, e.g.*, Leiter et al., *supra* note 30 (evaluating "the feasibility and utility of an internet-based crowdsourcing platform" for the development of clinical trials for metformin); Carol Cruzan Morton, *Innovating Openly*, IEEE PULSE, Jan.–Feb. 2014, at 63, 64 (discussing Transparency Life Sciences, LLC, website enlisting the assistance of researchers and patients to design clinical trials for Lisinopril, which was "the first investigational new drug application developed with the aid of crowdsourcing"); Michael Goodman, *Transparency Life Sciences Wants to Change How We Design and Execute Clinical Trials*, CLINICAL INFORMATICS NEWS (June 7, 2016), http://www.clinicalinformaticsnews.com/2016/6/7/transparency-life-sciences-wants-change-how-we-design-trials.aspx [http://perma.cc/5NFG-SHJN] (describing "patient centricity" through use of crowdsourced clinical trials); Laurie Halloran, *Re-thinking Clinical Trials for the World of Crowdsourcing*, XCONOMY (Apr. 16, 2013), https://www.xconomy.com/boston/2013/04/16/re-thinking-clinical-trials-for-the-world-of-crowdsourcing/ [https://perma.cc/K8J3-JTE8] (urging the life science industry to innovate by using crowdsourcing models).

33. *See, e.g.*, Assaf Gottlieb et al., *Ranking Adverse Drug Reactions with Crowdsourcing*, 17 J. MED. INTERNET RES. e80 (2015) (demonstrating use of internet-based crowdsourcing to rank adverse drug reaction severity); Jonah Comstock, *FDA Taps PatientsLikeMe to Test the Waters of Social Media Adverse Event Reporting*, MOBI HEALTH NEWS (June 14, 2015), http://www.mobihealthnews.com/44366/fda-taps-patientslikeme-to-test-the-waters-of-social-media-adverse-event-reporting [https://perma.cc/TZH6-BBE7] (discussing research partnership between the FDA and an online patient community); Dole Oleson, *Discovering Drug Side Effects with Crowdsourcing*, CROWDFLOWER (Mar. 21, 2013), https://www.crowdflower.com/discovering-drug-side-effects-with-crowdsourcing/ [https://perma.cc/W3ND-Z2CL] (detailing collection of tweets regarding the use of the drug Claritin for month of October 2012 that surpasses number of adverse events received by FDA).

34. *See, e.g.*, *Harnessing the Crowd*, *supra* note 10 (discussing the National Cancer Institute's crowdsourcing challenges); *GBM AGILE*, NAT'L BIOMARKER DEV. ALLIANCE, http://www.nbdabiomarkers.org/gbm-agile [https://perma.cc/8RV9-NCCG] (discussing a non-profit organization collecting biomarkers via crowdsourcing).

35. *See, e.g.*, Adrienne Burke, *Crowdsourcing Scientific Progress: How Crowdflower's Hordes Help Harvard Researchers Study TB*, FORBES (Oct. 26, 2011, 10:00 AM), https://www.forbes.com/sites/techonomy/2011/10/26/crowdsourcing-scientific-progress-how-crowdflowers-hordes-help-harvard-researchers-study-tb/#50d9f0865a12 [https://perma.cc/BSE2-69P5] (discussing crowdsourcing effort to analyze images of live cells involved in tuberculosis study); Nat'l Inst. of Allergy & Infection Diseases, *Crowdsourcing Platform Makes Public Gene Expression Data More Accessible*, SCI. DAILY (June 20, 2016), https://www.sciencedaily.com/releases/2016/06/160620120356.htm [https://perma.cc/RJ9P-ARQY?type=image] (detailing a new platform to assist gene expression computation); Clare Sansom, *Crowdsourcing Cancer Research: A Smartphone Game to Analyse Cancer Gene Data*, ECANCER (Feb. 6, 2014), http://ecancer.org/news/5227-crowdsourcing-cancer-research--a-smartphone-game-to-analyse-cancer-gene-data.php [https://perma.cc/UN99-5JYK] (detailing the specifications of a smartphone game launched by U.K. scientists).

36. News Release, Transparency Life Sci., LLC, FDA Clears IND for First Clinical Trial Protocol Developed Using Crowdsourcing (Dec. 18, 2012, 7:30 AM), http://www.prnewswire.com/news-releases/fda-clears-ind-for-first-clinical-trial-protocol-developed-using-crowdsourcing-183922651.html [https://perma.cc/ZKJ9-L3EQ].

community to solve targeted problems.[37] Challenges have been initiated by for-profit companies, health providers, disease foundations, and academics and are broadcast to a broad community.[38] Notable challenges in the life sciences include those in the realm of structural biology, genomics, systems biology, medicine, and data assessment and analytical tools.[39]

One concerted area of crowdsourcing that is experiencing rapid attention is that of NGS and biomarker development to inform cancer drug innovations. The 21st Century Cures Act defines a biomarker as "a characteristic (such as a physiologic, pathologic, or anatomic characteristic or measurement) that is objectively measured and evaluated as an indicator of normal biologic processes, pathologic processes, or biological responses to a therapeutic intervention."[40] Biomarkers can be categorized based on their purpose. Predisposition biomarkers assess an individual's risk of developing a particular disease; diagnostic biomarkers identify a specific disease; prognostic biomarkers serve to predict the course of disease in an individual; monitoring biomarkers monitor the progression of disease; and predictive biomarkers predict the response or reaction to a drug.[41] The 21st Century Cures Act also prioritizes cancer research and drug development. It appropriates $4.8 billion in funding to the National Institute of Health for the Precision Medicine Initiative and Cancer Moonshot 2020 over the next decade.[42] The hope is that discoveries fueled by NGS capabilities will identify genetic biomarkers critical for cancer screening and appropriate treatment based on an individual genetic profile.

There are very recent successes arising out of NGS and biomarker identification for cancer. As noted earlier, the FDA approved Merck's Keytruda (pembrolizumab) in May 2017 for the treatment of adult and pediatric patients with unresectable or metastatic solid tumors.[43] Patients who will respond favorably to Keytruda possess the microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) biomarker.[44] Likewise, NGS technology has enabled the development of medical devices to screen genetic samples for dozens of cancer mutations simultaneously, some of which have a corresponding approved

37. Saez-Rodriguez et al., *supra* note 10, at 470.

38. *Id.* at 471.

39. *Id.*

40. 21st Century Cures Act, Pub. L. 114-255, § 3011(a), 130 Stat. 1033, 1088–89 (2016).

41. MARKUS BÜCHELER ET AL., EUR. PERSONALISED MED. ASS'N, PERSONALISED MEDICINE IN EUROPE – ENHANCING PATIENT ACCESS TO PHARMACEUTICAL DRUG-DIAGNOSTIC COMPANION PRODUCTS 7 (2014), http://www.epemed.org/online/www/content2/104/107/910/pagecontent2/4339/791/ENG/EpemedWhitePaperNOV14.pdf [https://perma.cc/E9F8-293U].

42. 21st Century Cures Act § 1001(b)(4); U.S HOUSE OF REPRESENTATIVES COMM. ON ENERGY & COMMERCE, THE 21ST CENTURY CURES ACT 1 (2016, https://energycommerce.house.gov/sites/republicans.energycommerce.house.gov/files/documents/114/analysis/20161128%20Cures%20Fact%20Sheet.pdf [https://perma.cc/5NGM-HRVT]. The funding includes money for the BRAIN Initiative as well.

43. News Release, FDA, *supra* note 1.

44. *Id.*

drug.[45] These successful drug and medical device products currently on the market were evaluated and approved by the FDA, signaling the acceptance of NGS technology and of biomarkers as clinically meaningful measures of drug efficacy. The next Part explores the FDA's efforts to inform and guide NGS and biomarker development through the precisionFDA portal.

II. THE PRECISION FDA CROWDSOURCING PLATFORM

The introduction of the FDA's crowdsourcing platform, precisionFDA, coincided with President Obama's Precision Medicine Initiative, which aimed "to accelerate biomedical discoveries and provide clinicians with new tools, knowledge, and therapies to select which treatments will work best for which patients."[46] First announced in 2015, the Precision Medicine Initiative was subsequently expanded and infused with funding in the 21st Century Cures Act of 2016.[47] Efforts to construct an online community that allowed users to "test, pilot, and validate existing and new bioinformatics approaches for [the] processing" of NGS were begun in July 2014 by the FDA's Chief Informatics Office within the Office of Health Informatics.[48] A beta version of the website launched in December 2015.[49] As described on the website, precisionFDA provides a "private area where participants . . . can conduct genome analysis and comparison against reference material, and a community area where they can publish and share results, reference materials, and tools."[50] The online platform provides access to a variety of tools to assist users in efforts to increase accuracy and quality of NGS-based tests, including "reference sample[s] of DNA for [purposes of] validating human genome sequences [created] by the National Institute of Standards and Technology."[51] Users can compare results, share results, track changes to datasets, and get feedback from other users across a broad range of topics.[52]

---

45. *List of Cleared or Approved Companion Diagnostic Devices*, *supra* note 2; *see* Justin Petrone, *FDA Wades into Sequencing-Based Diagnostics Regulation*, 34 NATURE BIOTECHENOLOGY 681, 681 (2016).

46. Press Release, White House, FACT SHEET: President Obama's Precision Medicine Initiative (Jan. 30, 2015), https://obamawhitehouse.archives.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative [https://perma.cc/QBV8-67NE].

47. 21st Century Cures Act § 2011; *see also* Jordan Paradise, *Cultivating Innovation in Precision Medicine Through Regulatory Flexibility at the FDA*, 11 N.Y.U. J.L. & LIBERTY 672 (2017).

48. FDA, *About precisionFDA: Why? Background and Motivation*, PRECISIONFDA, https://precision.fda.gov/about/why [https://perma.cc/YNK8-DGAM]. Previously, in June 2014, the FDA launched openFDA, an online open-access portal for medical device information and data. *See About openFDA*, OPENFDA, https://open.fda.gov/about/ [https://perma.cc/KD52-QXS5].

49. FDA, *supra* note 48.

50. FDA, *About precisionFDA: What? A Genomics Community and Platform*, PRECISIONFDA, https://precision.fda.gov/about/what [https://perma.cc/2625-ULJV].

51. Taha Kass-Hout et al., *From Competition to Collaboration: precisionFDA Challenges*, U.S. FOOD & DRUG ADMIN.: FDA VOICE (May 19, 2016), https://blogs.fda.gov/fdavoice/index.php/tag/next-generation-sequencing-ngs/ [https://perma.cc/D4B8-PNA4].

52. *Id.*

A. Use and Functionality

The developer of the precisionFDA platform, DNAnexus, envisions users to be NGS-test providers, pharmaceutical and biotech companies, standard-setting institutions, health-care providers, academic medical centers, patient advocacy groups, and various research consortia.[53] Users must register to acquire full access to precisionFDA; visitors may also choose to acquire temporary access, allowing them to browse the site for 30 days. Users who request temporary access receive the following statement in an email along with a personal link:

> Note: PrecisionFDA is a beta regulatory research sandbox and is intended to inform a broad community. As you browse precisionFDA, you may become interested in obtaining a precisionFDA user account, in order to be able to actively contribute. In that case, please contact PrecisionFDA@fda.hhs.gov with your plan. Community members who have committed to providing information and programs that can be useful in our initial focus of NGS Clinical Test Development and Validation will be assessed for contributor level access.[54]

Upon basic access, the site provides options for users to access documentation and tutorials explaining the resources available and the scope of content. The top panel of the website displays icons denoting the different categories of resources. Those with temporary access may browse the site but cannot access all of the content.

Once users acquire an account, they are able to upload data and programming files to cloud storage.[55] Uploaded files can be used anywhere within precisionFDA (e.g., "downloaded, published, or provided as input" within applications).[56] There are both public (i.e., published) settings and private settings available on the website.[57] Users can access public files or attach their own files; furthermore, after clicking on a specific public file, users can also view notes, discussion threads, and comparisons run by users.[58] A key feature of precisionFDA is the ability of users to compare two data sets (in the variant call format) that evaluate NGS assays.[59] The comparisons are run with a test set and a benchmark set and users specify what genomic region to compare.[60] Several metrics are reported at the conclusion of a comparison including true and false

---

53. *DNAnexus to Deliver precisionFDA*, BUS. WIRE (Aug. 5, 2015, 1:52 PM), http://www.businesswire.com/news/home/20150805006334/en/DNAnexus-Deliver-precisionFDA [https://perma.cc/9Y7B-MYGY].

54. E-mail from precisionFDA, U.S. Food & Drug Admin., to Jordan Paradise, Professor of Law, Loy. Univ. Chi. School of Law (July 13, 2017, 2:35 PM) (on file with author).

55. FDA, *Files*, PRECISIONFDA, https://precision.fda.gov/docs/files [https://perma.cc/9328-5A24].

56. *Id.*

57. FDA, *Publishing*, PRECISIONFDA, https://precision.fda.gov/docs/publishing [https://perma.cc/UM2H-3HYZ].

58. FDA, *supra* note 55.

59. FDA, *Comparisons*, PRECISIONFDA, https://precision.fda.gov/docs/comparisons [https://perma.cc/T9BF-CWDF].

60. *Id.*

positives, false negatives, precision, recall sensitivity, and F-measure (i.e., accuracy).[61] Users can leave notes on their analysis or experimental designs in the notes section, generating discussions reflected in the open forum discussion threads.[62] Users are able to view public discussion participants who choose to publish their comments.[63]

Users can also access, manage, and share software applications by publishing them.[64] Again, public and private settings ensure that users can either develop their applications for their own use, or share publicly via the website.[65] The default application setting dictates that applications cannot access the internet of the users, which "increases user comfort and lowers the barriers for users to try out apps."[66] There is also a tracking feature within the website that that depicts all public revisions to an application.[67] Users can also choose to share software assets, which are described on the site as "building blocks" to application development.[68]

Users have already been challenged by the FDA to test the accuracy and reproducibility of software applied to genetic research through the online portal and to identify genetic variants within select datasets.[69] PrecisionFDA has posed four focused challenges to users: the Consistency Challenge that ran from February 2016 through April 2016, the Truth Challenge that ran from April 2016 to May 2016, the App-a-thon in a Box Challenge that ran from August 2016 to December 2016, and the Hidden Treasures-Warm Up Challenge that ran from July 2017 to September 2017.[70] Challenges are designed to advance quality standards to achieve accurate and consistent results in the context of genetic tests.[71] The results are published, and a winner is selected based on comparison

---

61. *Id.*

62. FDA, *Notes*, PRECISIONFDA, https://precision.fda.gov/docs/notes [https://perma.cc/HH7V-YGG5].

63. *Id.*

64. FDA, *Apps*, PRECISIONFDA, https://precision.fda.gov/docs/apps [https://perma.cc/SZ8U-82GK] ("Apps are, in essence, shell scripts that run inside a Linux virtual machine on the cloud, and which are designed to perform whatever specific task has been envisioned by the app author. Apps come with an I/O specification, a 'contract' that describes the kinds of inputs they receive and the kinds of outputs they are expected to generate."); FDA, *Creating Apps*, PRECISIONFDA, https://precision.fda.gov/docs/creating_apps [https://perma.cc/J34T-2C6Z] [hereinafter FDA, *Creating Apps*].

65. FDA, *Creating Apps*, *supra* note 64.

66. *Id.*

67. FDA, *Tracking*, PRECISIONFDA, https://precision.fda.gov/docs/tracking [https://perma.cc/8ESQ-2W2W].

68. FDA, *Creating Apps*, *supra* note 64.

69. *PrecisionFDA Wraps Up Second Challenge*, CLINICAL INFORMATICS NEWS (May 19, 2016), http://www.clinicalinformaticsnews.com/2016/5/19/precisionfda-wraps-up-second-challenge.aspx [https://perma.cc/F9TW-8U7V].

70. FDA, *Previous PrecisionFDA Challenges*, PRECISIONFDA, https://precision.fda.gov/challenges [https://perma.cc/BP9C-9CQS].

71. FDA, *PrecisionFDA: Hidden Treasures—Warm Up*, PRECISIONFDA, https://precision.fda.gov/challenges/1 [https://perma.cc/CC4Y-Q4MV].

metrics.[72] Participant users can then interact with each other and collaborate on future projects.[73]

The connection between the current use and functionality of precisionFDA and the regulatory process is as yet unclear. The FDA has published several draft guidance documents[74] and discussion papers[75] on analytical and clinical strategies to support the development of NGS diagnostic tests. FDA's Chief Health Informatics Officer describes precisionFDA "as a community rather than [as] a way to regulate."[76] As of July 2016, the website included 1,400 users from 600 organizations,[77] though it is not evident how users are contributing to the platform or whether specific products have been developed using the public information. Stated long-term goals for precisionFDA include standard development and best practices for NGS bioinformatics.[78]

B. Legal Disclaimers and Terms

Use of the website is not without limitations and legal specifications. Before a user logs into the website, the following disclaimer appears at the bottom of the page:

> By logging into precisionFDA, you are accessing a U.S. Government information system. Usage of precisionFDA may be monitored, recorded, and subject to audit. Your use of precisionFDA indicates your consent to monitoring and recording of precisionFDA usage, and if such monitoring reveals possible criminal activity, precisionFDA personnel may provide such monitoring as evidence to law enforcement officials. Any unauthorized use of the system is prohibited and subject to criminal and civil penalties.[79]

The precisionFDA website also contains both the Terms of Service and a link to the FDA website housing both the Privacy Policy and Disclosure Policy.

---

72. *Id.*

73. *See id.*

74. The FDA has expressed that they are "committed to implementing a flexible and adaptive regulatory oversight approach" for NGS *in vitro* diagnostics. *See* FDA, USE OF STANDARDS IN FDA REGULATORY OVERSIGHT OF NEXT GENERATION SEQUENCING (NGS)-BASED IN VITRO DIAGNOSTICS (IVDS) USED FOR DIAGNOSING GERMLINE DISEASES, DRAFT GUIDANCE FOR STAKEHOLDERS AND FOOD AND DRUG ADMINISTRATION STAFF 2 (2016) [hereinafter DRAFT GUIDANCE: USE OF STANDARDS].

75. *See, e.g.*, FDA, DEVELOPING ANALYTICAL STANDARDS FOR NGS TESTING (2015), https://wayback.archive-it.org/7993/20170406192845/https://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM468521.pdf; FDA, O PTIMIZING FDA'S REGULATORY OVERSIGHT OF NEXT GENERATION SEQUENCING DIAGNOSTIC TESTS-PRELIMINARY DISCUSSION PAPER (2015), https://www.fda.gov/downloads/medicaldevices/newsevents/workshopsconferences/ucm427869.pdf; FDA, USE OF DATABASES FOR ESTABLISHING THE CLINICAL RELEVANCE OF HUMAN GENETIC VARIANTS (2015), https://wayback.archive-it.org/7993/20170406192846/https://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM467421.pdf.

76. Petrone, *supra* note 45, at 682.

77. *Id.*

78. *Id.*

79. FDA, *Log In*, PRECISIONFDA, https://platform.dnanexus.com/login?scope=%7B%22full%22%3A+true%7D&redirect_uri=https%3A%2F%2Fprecision.fda.gov%2Freturn_from_login&client_id=precision_fda_gov [http://perma.cc/W4GH-2K7R].

Notably, the first sentence in the terms of service states that "[p]recisionFDA is a beta research project and not for clinical use."[80] The terms further provide that "[u]se of the services made available via PrecisionFDA is restricted to usage specifically related to the FDA's PrecisionFDA program as determined by the FDA."[81] The FDA grants "[u]sers a nonexclusive, nontransferable, revocable, limited license during the term of [the] Agreement to access and use and to authorize Users to access and use the Services to transfer, store, process, analyze, and display User Data in performing PrecisionFDA-related tasks."[82] Users cannot "copy, translate, modify, adapt, enhance, decompile, disassemble or reverse engineer" anything within precisionFDA, with the exception of the software that is distributed under a free open-source license.[83] Users are not allowed to grant third party access to anything within precisionFDA nor sell, rent, transfer or make anything from precisionFDA available to third parties.[84] Users also agree not to add third party information to the site without appropriate approval, nor will they add Protected Health Information (PHI) and Personally Identifiable Information (PII) without all necessary permissions and informed consents.[85] The FDA agrees that they shall not access any information that is contained solely in a private space and that they will maintain the security of the site consistent with industry standards.[86]

The short intellectual property (IP) portion of the agreement states that there are no IP rights either implied or otherwise granted to either party; however, it does provide that the user "grants FDA a nonexclusive, nontransferable, revocable, royalty-free, limited license . . . to access and use . . . IP solely for . . . delivering [s]ervices."[87] The user data section of the agreement also instructs that users are not to store confidential commercial information in a way that makes it "accessible to all [u]sers";[88] nor are users to "store [t]rade [s]ecrets on PrecisionFDA."[89] Notably absent is any express requirement in the terms of service that a user attribute precisionFDA in publications or place those publications in the public domain.

The FDA's online privacy policy explains that the FDA collects two types of information: information voluntarily entered and information automatically collected.[90] The automatically collected information includes a user's computer IP address, the user domain from which the website was accessed, the website

80. FDA, *Terms of Service*, PRECISIONFDA, https://precision.fda.gov/terms [http://perma.cc/K63F-YWXP] (last modified Oct. 30, 2015).

81. *Id.*

82. *Id.* § 1.1 (License).

83. *Id.* § 1.2 (Restrictions).

84. *Id.* § 1.2.4 (Restrictions).

85. *Id.* §§ 2.1–2.4 (User Data).

86. *Id.* § 3 (Privacy and Security).

87. *Id.* § 5.1 (Intellectual Property).

88. *Id.* § 2.5 (Confidential Commercial Information).

89. *Id.* § 2.6 (Trade Secrets).

90. *Website Policies*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/AboutFDA/AboutThisWebsite/WebsitePolicies/default.htm [https://perma.cc/F9WE-TW67] (last updated Dec. 29, 2017).

that redirected the user to precisionFDA or other FDA websites, the date and time the user accessed the site, the length of time the user remained on the site, the name and version of the user's computer operating system, and the pages visited.[91] The website disclosure policy further provides that the "FDA will not disclose, give, sell, or transfer any personally identifiable information (PII) about . . . visitors unless it is required . . . [b]y law or regulation [or] [f]or law enforcement reasons."[92]

Users of precisionFDA are able to attach license agreements to any of their public contributions.[93] License agreements may cover topics such as usage restrictions, waiver of liability, insurance indemnification, publication embargoes, assignment, and ownership of intellectual property.[94] The FDA assures that all user licenses are published and publicly available in connection with the public files; therefore, any user who accepts the licensing terms and opens the file is subject to those licensing terms.[95] Users must agree to those terms by clicking the "accept license" button at the top right of the page to access the files.[96] However, it appears that the user need not even open the license to accept the terms. After an item has been published with the license, users can manage and view who has accepted the license and subsequently block individual users.[97] The website has a model license agreement posted in the tutorial section of the materials within the licensing description.[98]

Overall, precisionFDA users are thus subject to several layers of legal documents originating from the FDA: the general disclaimer, the Terms of Service, the Privacy Policy, and the Disclosure Policy. Users may also be subject to individual licensing agreements for use of particular applications or files, which are developed by outside parties.

III. LEGAL AND REGULATORY IMPLICATIONS

Scholars have just begun to assess the vast range of legal issues associated with crowdsourcing models as a general matter. These legal issues span various traditionally recognized areas, including contract law, securities law, insurance law, data privacy and confidentiality, employment law, IP law, and potentially gaming law.[99] When looking to the use of NGS crowdsourcing in medicine and

---

91. *Id.*

92. *Id.*

93. FDA, *PrecisionFDA: Licenses*, PRECISIONFDA, https://precision.fda.gov/docs/licenses [https://perma.cc/NPC2-FYKQ].

94. *Id.*

95. *Id.*

96. *Id.*

97. *Id.*

98. *Id.* (UCSF-Stanford CERSI, *PrecisionFDA: How to Use the Licensing* Feature, YOUTUBE (July 6, 2016), https://www.youtube.com/watch?time_continue=15&v=7iwwnKmalyM).

99. For a discussion of these issues see, for example, Alek Felstiner, *Working the Crowd: Employment and Labor Law in the Crowdsourcing Industry*, 32 BERKELEY J. EMP. & LAB. L. 143 (2011); Henri Simula, *The Rise and Fall of Crowdsourcing?*, *in* PROCEEDINGS OF THE 2013 46TH HAWAII INTERNATIONAL CONFERENCE ON SYSTEM SCIENCES 2783, 2788 (2013); Stephen M. Wolfson & Matthew Lease, *Look Before You Leap: Legal Pitfalls of Crowdsourcing*, 48 PROC.

life sciences, the pressing legal questions chiefly revolve around the IP status of the information shared and collected, as well as the regulatory implications, given the lucrative potential of discoveries and innovations in the life sciences.

The new platform developed for the FDA is in early rollout phases and uncertainty exists about its long-term purposes. As noted earlier, the website is limited in functionality and accessible in full format only after individuals secure a username and password.[100] Although the FDA has issued several user challenges and has provided tools and app-sharing mechanisms, it is unclear how the FDA will continue to support the platform, or how the agency may begin to integrate crowdsourced information into their contemplation of appropriate regulation and standard setting. Reflecting on the attributes of the precisionFDA platform coupled with the legal provisions described in Part II, this Part offers several modest insights on the relationship to regulatory review and approval, as well as possible IP implications.

First, at the regulatory level, the FDA will need to determine how to integrate crowdsourced information into the regulatory process, if at all. The FDA is approving drugs, assessing NGS-based tests, and reviewing biomarker discoveries resulting from prevision medicine initiatives. Guidance from the agency acknowledges that standard-setting efforts will rely largely on information and data collected from drug and device sponsors.[101] Recent legislation also presses the agency to take into consideration "real world evidence" and "patient experience data" when reviewing new drug applications.[102] It is unclear what threshold of reproducibility, validity, and reliability will be necessary to achieve standard-status for a particular biomarker or when information gathered and shared on the FDA-sponsored site may be relevant to regulatory review for a given product.

The FDA also needs to consider foreseeable issues with regard to the validity and reliability of the public information available through the online platform, and how information shared through the platform is maintained. Will, or should, the FDA have a role as gatekeeper and monitor? While many may advocate that the online community is well suited to regulate its behavior, this may not be true. Although the users are typically generalized as researchers and scientists—regardless of private or public affiliation—different disciplines inevitably hold varying viewpoints and norms on aspects of attribution, sharing, and collaboration. There may be opportunities for data trolls to break down the synergistic crowdsourcing community using the shared platform. There may also be concerns about protection of the information submitted and maintained on the online platform, potentially with sensitive privacy issues relating to de- and re-identification of shared data.

ASS'N FOR INFO. SCI. & TECH. 1 (2011); Lieberstein et al., *supra* note 21, at 35; Marc Lieberstein & Ashford Tucker, *Crowdsourcing and Intellectual Property Issues*, ASS'N CORP. COUNS. (Aug. 29, 2012), http://www.acc.com/legalresources/quickcounsel/caipi.cfm [https://perma.cc/5Y2S-5CQR].

100. *See* discussion *supra* Sections II.A, II.B.

101. *See* DRAFT GUIDANCE: USE OF STANDARDS, *supra* note 74.

102. 21st Century Cures Act, Pub. L. 114-255, §§ 3001–004, 3022, 130 Stat. 1033, 1083–85, 1096–97 (2016).

Second, users contributing to the website and participating in the challenges imposed by the FDA should consider the implications of these activities on ownership and access rights. While the FDA supplies privacy, security, and disclosure policies for users, individual contributors are able to publish licensing agreements and other terms relating to access to their materials. As use and traffic on the website increases, relationships will be created through contract law as users agree to select terms for use of information. It is likely that litigation will soon arise pitting precisionFDA users against each other. For example, a scenario may arise in which a license agreement will be challenged once a tangible product, whether a drug based on a biomarker identified through crowdsourcing efforts or an NGS-based test, is in existence and someone is seeking a patent or FDA approval and exclusivities. Depending on the product, different elements of the platform materials and activities will be relevant, including software aspects developed as an application, identification and analysis linked to a particular biomarker, or a detection device itself integrating software and biomarker attributes. A court will need to interpret the licensing agreement and the relationships involved under contract law principles. Much of this assessment will scrutinize the ownership and IP provisions, and terms of use.

Third, tied to questions of ownership and access framed in contract and licensing terms, are IP issues. In particular, what contributions will be recognized by patent law? In the United States, a patent is awarded for inventions that are novel, useful, nonobvious, and are adequately enabled by the written description contained within the patent application.[103] The Leahy-Smith America Invents Act introduced a first-to-file system in the United States, where the first inventor to file an application achieves inventor status as long as the other subjective patent law requirements are met.[104] There are also questions of joint inventorship raised by NGS crowdsourcing.[105] The federal patent law recognizes that individuals working in different locales, at different times, and in different proportions relative to the whole of the invention may be joint inventors.[106] All inventors must be named on the patent application, and once granted a patent can be invalidated for failure to name a coinventor.[107] Much litigation has focused on teasing out who is a proper inventor.

Crowdsourcing may force a wholesale restructuring of traditional intellectual property frameworks in biomedical research. With numerous actors working on a scientific challenge, several incremental "inventions" may result in a patent-worthy outcome across a national or international network. The U.S. Patent & Trademark Office should begin to examine these issues and proactively develop an approach to joint inventorship or proportional inventorship rights.

---

103. 35 U.S.C. §§ 101, 102, 103, & 112 (2012).

104. Leahy-Smith America Invents Act, Pub. L. No. 112-29, § 3, 125 Stat. 284, 285 (2011).

105. *See, e.g.*, Wolfson & Lease, *supra* note 99, at 4.

106. 35 U.S.C. § 116 (2012). For a discussion of joint inventorship requirements and scope, see Jordan Paradise, *Patient Advocacy Group Collaboration in Genetic Research and the Scope of Joint Inventorship Under U.S. Patent Law*, 3 INT'L J. INTELL. PROP. MGMT. 97 (2009).

107. Paradise, *supra* note 106, at 103.

Online communities also continue to share resources online, establishing open source databases and networks of tools for scientists. Such open source platforms are a direct response to monopolistic patent rights, which reserve the rights to use and sell in the patent holder alone for a limited time. Open source efforts such as the BioBricks Foundation—in the realm of synthetic biology—provide an innovative example of a biology commons to avoid the stifling effect of patent rights.[108] As research moves in the direction of open source, the intellectual property protections change. Many question whether there is a role for non-patent incentives in the life sciences and biomedical research, which will prove to be part of an ongoing debate.

The FDA has provided the life science research and scientific community with an invaluable resource through the precisionFDA platform. Launched in December 2015, precisionFDA allows private and public actors to contribute towards solving complex scientific problems arising out of NGS and genomic research. The agency is also exploring additional crowdsourcing mechanisms to inform NGS exploration and product development. As NGS crowdsourcing continues, legal and ethical questions will undoubtedly emerge in the life science industry. Many of these questions will involve the application of IP law principles and regulatory review by the FDA. This article has explored the FDA's recently launched crowdsourcing platform, precisionFDA, and offers initial modest thoughts on some of the regulatory implications.

108. *About the BioBricks Foundation*, BIOBRICKS FOUND., https://biobricks.org/ [https://perma.cc/ZUT8-893Z] (BioBricks Found., *BioBricks: Our Mission*, YOUTUBE (Aug. 10, 2016), https://www.youtube.com/watch?v=UhlqN1z9UrI).