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Information Opacity in Biopharmaceutical Innovation Through the Lens of COVID-19

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I. INTRODUCTION

The COVID-19 pandemic has revealed myriad and complex challenges for our national health care system spanning preparedness, response, access, costs, infrastructure, coordination, and medical innovation. These challenges implicate federal, state, and local agencies and actors, as well as international collaborative bodies. One constant throughout the pandemic has been the pressing need for safe and effective diagnostics, prophylactic vaccines, and drug treatments to counter the virus.[1] Inarguably, significant problems with the multi-faceted system of drug and vaccine innovation and regulation manifested long before the COVID-19 pandemic.[2] The pandemic, however, has laid bare the inextricable connections among federal funding, patents, product review and approval mechanisms, and the eventual medical products and resulting costs.

As a mechanism to assure positioning in a competitive marketplace, pharmaceutical and biotechnology companies rigorously protect their patents claiming the compounds, methods, and processes pertaining to their products approved by the U.S. Food and Drug Administration ("FDA").[3] Often, these patents are achieved through substantial governmental funding for the basic research leading to the patent.[4] Scholarly literature and media reports are rife with these stories of patent protectionism pre-COVID.[5] Federal agencies, industry competitors, and state attorneys general spend billions of dollars challenging industry behavior through administrative and legal actions each year.[6]

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[1]*See* Ralph Weissleder et al., *COVID-19 Diagnostics in Context,* 12 Sci. Translational Med. 1, 2 (2020) (comparing COVID-19 test types); J.S. Tregoning et al., *Vaccines for COVID-19*, 202 Clinical and Experimental Immunology 162, 168-173 (2020) (comparing COVID-19 vaccines); James M. Sanders et al. *Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19): A Review*, 323 JAMA 1824, 1826-1828 (2020) (comparing COVID-19 treatments).

[2]Ohid Yaqub & Paul Nightingale, *Vaccine Innovation, Translational Research and the Management of Knowledge Accumulation*, 75 Soc. Sci. & Med. 2143 (2012).

[3]Dmitry Karshtedt, *The More Things Change: Improvement Patents, Drug Modifications, and the FDA*, 104 Iowa L. Rev. 1129 (2019).

[4]Wendy H. Schacht, Cong. Res. Serv., RL32076, The Bay-Dole Act: Selected Issues in Patent Policy and the Commercialization of Technology (Dec. 3, 2012), https://fas.org/sgp/crs/misc/RL32076.pdf [https://perma.cc/H9EM-8TJP].

[5]*See, e.g.,* Jordan Paradise, *REMS as a Competitive Tactic: Is Big Pharma Hijacking Drug Access and Patient Safety?,* 15 Hous. J. Health L. & Pol'y 43, 43 (2015).

[6]*See* James E. Bessen & Michael J. Meurer, *The Private Costs of Patent Litigation*, 9 J.L. Econ. & Pol'y 59 (2012); Brian J. Love & James Yoon, *Predictably Expensive: A Critical Look at Patent Litigation in the Eastern District of Texas*, 20 Stan. Tech. L. Rev. 1 (2017).

Judges scrutinize these legal challenges and render their decisions after years of expensive and time-consuming litigation.[7] Only a select few of these cases achieve review by the Supreme Court.[8] Regrettably, those holdings often prove controversial for, among other things, ostensibly failing to identify a clear standard for the lower courts or agencies to apply, overturning decades of federal circuit precedent, effectively invalidating immeasurable patent claims, or decreeing retrospective application.[9] This pattern has persisted for decades, with the pharmaceutical industry adeptly adjusting to the resultant ebb and flow of case law and agency adjudication, congressional legislation and investigations, agency rulemaking and policy, and changing market conditions.[10]

The reason for these complex and long-standing problems derives somewhat from the design of the complex statutory frameworks at play. Yet, alongside the express statutory directives, there is an elusiveness to informational obligations, a lack of publicly available information on the path from discovery to market, and a systemic failure of key agencies to endeavor to communicate with each other as they pursue their missions. The current tangled network of agency authority and the piecemeal and iterative response to perceived bad behavior on the part of the pharmaceutical industry has consistently failed the health care system and the American public.[11] Reactive and incremental changes to the relationship among FDA regulation, federal funding of research, pharmaceutical patents, and industry behavior, through mechanisms of federal legislation, case law, and agency rulemaking, have exacerbated the problems.[12]

These systemic, structural failures must be addressed alongside the implementation of a functioning mechanism to assimilate the chronology of National Institutes of Health ("NIH") and other federal research funding, the United States Patent and Trademark Office's ("PTO") patent review and issuance, and the FDA's regulation of tangible

[7]Amy Semet, *Specialized Trial Courts in Patent Litigation: A Review of the Patent Pilot Program's Impact on Appellate Reversal Rates at the Five-Year Mark*, 60 B.C. L. Rev. 519 (2019).

[8]Federal Trade Commission v. Actavis, 570 U.S. 136 (2013).

[9]Greg Reilly, *How Can the Supreme Court Not Understand Patent Law*, 16 Chi.-Kent J. Intell. Prop. 292 (2016).

[10]One particularly illustrative example is Allergan's 2017 transfer of their Restasis patent portfolio to a Native American tribe in a judicially thwarted attempt to avoid *inter partes* review at the United States Patent and Trademark Office initiated by a competitor. Saint Regis Mohawk Tribe, Allergan Inc. v. Mylan Pharmaceuticals, 896 F.3d 1322 (Fed. Cir. 2018). "Inter partes review is a trial proceeding conducted at the Board to review the patentability of one or more claims in a patent only on a ground that could be raised under §§ 102 or 103, and only on the basis of prior art consisting of patents or printed publications." U.S. Patent & Trademark Off., *Inter Partes Review*, https://www.uspto.gov/patents-application-process/appealing-patent-decisions/trials/inter-partes-review [https://perma.cc/Y69C-EETZ]. The Federal Circuit ultimately held that sovereign immunity status of the tribe did not prevent such review; the Supreme Court subsequently denied certiorari. Saint Regis Mohawk Tribe, Allergan Inc., 896 F.3d 1322 (Fed. Cir. 2018), *cert. denied*, No. 18-899, 2019 WL 1590253 (Apr. 15, 2019).

[11]The original Pure Food and Drug Act was enacted in 1906, with myriad legislative amendments over the ensuing 115 years. One piece of legislation of direct relevance to this article is the Hatch-Waxman Act of 1984, codified at 21 U.S.C. § 355, establishing the generic drug approval process and related patent certification and listing provisions discussed *infra,* Part IV. A second is the Biologic Price Competition and Innovation Act of 2010, codified at 42 U.S.C. § 262 et seq., and discussed *infra*, Part IV.

[12]There is a vast landscape of legal scholarship exploring different aspects of these issues, particularly tied to innovation policy. This brief symposium article will not reprise that scholarship but notes its continued importance. *See, e.g,* W. Nicholson Price & Arti K. Rai, *Manufacturing Barriers to Biologics Competition and Innovation*, 101 Iowa L. Rev. 1023 (2015); Rebecca S. Eisenberg, *Patents, Product Exclusivity, and Information Dissemination: How Law Directs Biopharmaceutical Research and Development*, 72 Fordham L. Rev. 477 (2003); Rebecca Eisenberg, *The Role of the FDA in Innovation Policy*, 13 Mich. Telecom. Tech. L Rev. 345 (2007); Colleen V. Chien, *Cheap Drugs at What Price to Innovation: Does the Compulsory Licensing of Pharmaceuticals Hurt Innovation*, 18 Berkeley Tech. L.J. 853 (2003); Rebecca S. Eisenberg, *The Shifting Functional Balance of Patents and Drug Regulation*, 20(5) Health Aff. (Sep. 2001).

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products and disclosure mechanisms to support further innovation. Strategically homing in on this key regulatory interaction among the NIH, the PTO, and the FDA may provide a more targeted, adaptive, and effective means to address interrelated issues of exorbitant drug costs, price transparency, invalid or unenforceable patents, and widespread anticompetitive industry tactics. Though the pandemic has illuminated good actors as well, the resounding, collective message is that significant problems exist in our current system of medical product innovation.

This Article explores COVID-19 developments through the lens of individual and collaborative functioning of the three agencies chiefly responsible for the innovation of new medical products through funding, patents, and product approval. The common thread that emerges among all three agencies is a universal lack of transparency in the methods and means of performing select functions, and the resulting information inefficiencies that impact access, cost, and competition. The following chronological depiction of the route from research to market entry will guide this Article in identifying key agency responsibilities and opportunities to improve information inefficiencies and transparency problems.

BioX has developed a promising novel COVID-19 vaccine under stringent laboratory conditions. The vaccine could be a traditional biologically derived vaccine or one that is synthetic, such as a messenger RNA ("mRNA") vaccine. BioX files one or more patent applications with the PTO for the vaccine composition and production methods to secure first in time invention status. Although BioX received funding from the NIH for early-stage research, the patent application omits that fact and there is no universal recordkeeping mechanism available to track funding as related to specific patents. Meanwhile, BioX consults with the FDA to begin clinical trials, utilizing rapid-time mechanisms available for breakthrough and emergency therapies to treat or mitigate the effects of COVID-19. The FDA green-lights the clinical trials after review of protocols and assurances of safety, and works closely with BioX as data is aggregated. After accumulating promising, although limited, data demonstrating one hundred percent effectiveness in preventing severe cases of COVID-19 and ninety-four percent effectiveness in preventing infection, BioX submits a request for an Emergency Use Authorization ("EUA") with the FDA.

The EUA is granted following advisory committee meetings and BioX may now distribute the vaccine subject to manufacturing and quality controls, proper labeling and warnings, and other requirements. However, publicly available information regarding the safety and efficacy, chemistry, manufacturing, and controls associated with the EUA is limited. In the future, after longitudinal data develops, and with the FDA's guidance and input, BioX may then apply for a Biologic License Application ("BLA") for full approval of the vaccine, including the full clinical investigations supporting safety and efficacy that are made publicly available on the FDA's website after approval. Developers of biologics, such as vaccines, are not required to submit patent information to the FDA for publication and thus pending and awarded patents for biologics are not made publicly available in the application if they are the innovator or first product. Given variation in the legislative frameworks, however, if the product was instead a new drug, BioX would be obligated to disclose pending and awarded patents as part of the application, which the FDA would then publish as a public resource.

II. PANDEMIC FUNDING TRANSPARENCY

As international research and development efforts for promising COVID-19 vaccines and treatments escalated, conversations emerged in the United States about the impact

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of federal funding and intellectual property protections.[13] Long-standing legislation establishing systems for funding and licensing of inventions, coupled with an infusion of new monies and incentives through the Coronavirus Aid, Relief, and Economic Security ("CARES") Act[14] and Operation Warp Speed ("OWS"),[15] fueled discussions about access, cost, and ownership.[16] The Bayh-Dole Act of 1980 established the framework for public-private partnerships in the conduct and funding of research.[17] Where there is federal funding, the inventor and assignee institution are presumed to hold legal title to the patent, and the U.S. government retains a nonexclusive, nontransferable, and irrevocable license to the invention.[18] The government's license cannot be unilaterally revoked by the assignee institution and inventor, and the government can authorize a third party on behalf of the United States to use the patented invention without compensation to the patent holder.[19]

The Bayh-Dole Act also authorizes the government to "require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants upon terms that are reasonable" for any government-funded research that has led to the patent, when essential.[20] This provision provides so-called "march-in rights" that give the government the authority to manage and regulate the licensing of particular patented products that resulted from a federally-funded invention. These march-in rights may be exercised where there has been a lack of effort to commercialize within an agreed upon timeframe, if a specific timeframe for development was included in the original funding agreement between the government and the contractor, or when the "action is necessary to alleviate health or safety needs."[21] The law does not explain the scope of the "necessary to alleviate health or safety needs" clause and the U.S. government has never exercised its march-in rights contained in the Bayh-Dole Act.[22]

The COVID-19 pandemic has revitalized criticisms of the Bayh-Dole Act and the government's failure to utilize march-in rights to protect the public health.[23] The first FDA-approved treatment for complications arising from the novel coronavirus, remdesivir, sold under the brand name Veklury, has at least two patents associated with the drug.[24]

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[13]*See e.g.,* Ana Santos Rutschman, *The COVID-19 Vaccine Race: Intellectual Property, Collaboration(s), Nationalism and Misinformation*, 64 WASH. U. J. L. & POL'Y 167 (2021).

[14]Coronavirus Aid, Relief, and Economic Security Act or the CARES Act, H.R. 748, 116th Cong. (2020).

[15]*Fact Sheet: Explaining Operation Warp Speed*, HHS.GOV (Aug. 7, 2020), http://web.archive.org/web/20200807210537/https://www.hhs.gov/about/news/2020/08/07/fact-sheet-explaining-operation-warp-speed.html [hereinafter *Fact Sheet: Explaining Operation Warp Speed*].

[16]*See e.g.,* Anand Shah et al. *Unwavering Regulatory Safeguards for COVID-19 Vaccines* 324 JAMA 931 (2020); Kevin Volpp et al. *Behaviorally Informed Strategies for a National COVID-19 Vaccine Promotion Program* 325 JAMA 125 (2021).

[17]Bayh-Dole Act of 1980, 35 U.S.C. § 200 (1980).

[18]Jordan Paradise, *COVID-IP: Staring Down the Bayh-Dole Act with 2020 Vision,* 7 J.L. & THE BIOSCIENCES 1 (2020). The Act provides for exceptional circumstances where this presumption of inventorship can be rebutted.

[19]*See e.g.,* Anand Shah et al. *Unwavering Regulatory Safeguards for COVID-19 Vaccines* 324 JAMA 931 (2020); Kevin Volpp et al. *Behaviorally Informed Strategies for a National COVID-19 Vaccine Promotion Program* 325 JAMA 125 (2021).

[20]Bayh-Dole Act of 1980, 35 U.S.C. § 200 (1980).

[21]35 U.S.C. § 203 (2018).

[22]For a detailed discussion of prior petitions to the U.S. government to exercise these rights, *see* Paradise, *supra* note 18.

[23]*See* Paradise, *supra* note 18.

[24]Rapid Viral Assay, U.S. Patent No. 10,844,442 (filed May 18, 2020) (issued Nov. 24, 2020); Method of Treating, Reducing, or Alleviating a Medical Condition in a Patient, U.S. Patent No. 10,925,889 (filed Apr. 28, 2020) (issued Feb.23, 2021).

The U.S. government has contracted for much of remdesivir's supply and Gilead Sciences ("Gilead"), the drug's developer, has entered into manufacturing and supply deals with manufacturers to secure a global supply chain.[25] A five-day course of the drug costs $2340.[26] The price tag has been heavily rebuked, and commentators urge that in the face of a public health emergency such as COVID-19, the drug should be broadly available at low or no cost.[27] At least two patents protect the drug.[28] Issued in 2017 and 2018 to Gilead by the PTO, neither patent identifies funding by the U.S. government, although the patents reference collaborations and contributions of scientists at the Centers for Disease Control and Prevention and the Army Medical Research Institute for Infectious Disease.[29] Additional publications disclose collaborations between Gilead and government scientists on related research.[30]

In August 2020, California and Louisiana led a campaign on behalf of state attorneys general to call on the Secretary of Health and Human Services ("HHS") and the NIH to exercise march-in rights for remdesivir.[31] The letter, signed by thirty-four states attorneys general, pleads that Gilead has "fail[ed] to achieve a reasonable price or fail [ed] to reasonably 'alleviate health or safety needs' of consumers."[32] As the basis for the government to march-in, the letter references approximately $30 million of NIH funding to Gilead for a clinical trial in 2020.[33] Notably, drawing from various public sources, Public Citizen estimates that the federal government has provided at least $70.5 million in funding for the research leading to remdesivir.[34] The letter's requests have not been acted upon by the federal government, though a representative of the Trump Administration stated:

> We can only exercise march-in rights where the intellectual property to make the product, as a whole was funded by the federal government … . In short, all of the patents underlying the product have to have been conceived or reduced to practice with federal funds for Bayh-Dole's

[25]Valerie Bauman, *States Demand Gilead Drug Seizure Misread Law, Attorneys Say*, Bloomberg Law (Aug. 6, 2020) https://news.bloomberglaw.com/health-law-and-business/states-demanding-gilead-drug-seizure-misread-law-attorneys-say [https://perma.cc/VGP3-AFZD].

[26]Jacqueline Howard, *Here's How Much COVID-19 Drug Remdesivir Will Cost*, CNN (June 29, 2020), https://www.cnn.com/2020/06/29/health/remdesivir-cost-coronavirus-treatment-bn/index.html [https://perma.cc/5FJM-PT3L].

[27]*See* Bauman, *supra* note 25.

[28]The cost of the drug may fairly be related to the cost to manufacture, the utility of the treatment, or the absence of competitors on the market, rather than the patent itself. Whatever the reason, the cost has raised controversy. But because of a dearth of available information, the reasons for the cost are largely shrouded from the public. *See, e.g.,* Christopher Roland, *Taxpayers Paid to Develop Remdesivir But Will Have No Say When Gilead Sets the Price*, Wash. Post (May 26, 2020), https://www.washingtonpost.com/business/2020/05/26/remdesivir-coronavirus-taxpayers/ [https://perma.cc/5RKA-V25P].

[29]For a discussion of the contributions by federal researchers, *see* James Krellenstein & Christopher J. Morten, *The U.S. Government's Ownership of Patents Protecting Remdesivir,* N.Y.U. Clinical L. Ctr, Tech. L. & Pol'y Clinic White Paper (May 22, 2020).

[30]Justin Hughes & Arti K. Rai, *Acknowledging the Public Role in Private Drug Development: Lessons From Remdesivir*, STAT (May 8, 2020), https://www.statnews.com/2020/05/08/acknowledging-public-role-drug-development-lessons-remdesivir/ [https://perma.cc/4JW8-ZE8A].

[31]Letter from Xavier Becerra, California Attorney General, and Jeff Landry, Louisiana Attorney General, to Alex M. Azar, Secretary, Dep't of Health & Hum. Servs., Francis S. Collins, Director, National Institutes of Health, and Stephen Hahn, Commissioner, U.S. Food & Drug Admin. (Aug. 4, 2020), (available at https://www.oag.ca.gov/system/files/attachments/press-docs/Remdesivir%20Letter%2020200804.pdf [https://perma.cc/JBG5-ELYQ]).

[32]*Id.* at 2.

[33]*Id.* at 3.

[34]Public Citizen, *The Real Story of Remdesivir* (May 7, 2020), https://www.citizen.org/article/the-real-story-of-remdesivir [https://perma.cc/447W-AGNF].

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> march-in provision to be of any practical significance. We do not believe that to be the case here.[35]

Gilead, however, swiftly issued a statement of "disappointment" in response to the letter from the attorneys general, referencing numerous perceived errors and misrepresentations.[36] Gilead noted a corporate investment of $1 billion to expand manufacturing capacity to enable a fifty-fold increase in supply, which the company says will bring significant savings to hospitals, patients, and the health care system.[37] Gilead also stated that the use of march-in rights is not only unauthorized under the circumstances but it is also ineffectual to speed access to remdesivir, given a calculated six- to twelve-month lead time for ramping up manufacturing capabilities.[38]

The scope of the U.S. government's power under 28 U.S.C. section1498, allowing governmental patent use, is also an area of attention during the pandemic. Sixteen senators urged the Trump Administration to act through compulsory licensing authorities to contract with producers and manufacturers to produce remdesivir at lower or no cost.[39] This provision has been invoked by the government in the past to address drug shortages and military equipment.[40] The language of 28 U.S.C. section1498 provides that when a patented invention is "used or manufactured by or for the United States without license of the owner" the patent owner has the ability to bring suit against the United States for "recovery of his reasonable and entire compensation for such use and manufacture."[41] When this authority is exercised, the government need not have funded the patented invention; it applies broadly to all patents issued in the United States, regardless of whether the government was involved. The government has likewise not utilized this authority for COVID-19 patents in the wake of urging from legislators.

The extent of COVID-specific funding is also a source of increased scrutiny by public health officials, state and federal legislators, and other stakeholders examining the federal government's role in innovation in light of the pandemic.[42] Many critics are

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[35]This quote is from a secondary source, citing "an HHS spokesperson." The author cannot identify a primary source of the Trump Administration's response. Bauman, *supra* note 25. A second article cites STAT for the quoted correspondence from the HHS spokesperson. Joseph Allen, *No, You Can't March in on Remdesivir*, IPWatchdog.com (Aug. 6, 2020), https://www.ipwatchdog.com/2020/08/06/no-cant-march-remdesivir/id=123868/ [https://perma.cc/89GK-QZ3U].

[36]*Gilead Sciences Statement on State Attorneys General Letter on Remdesivir*, Gilead (Aug. 5, 2020), https://www.gilead.com/news-and-press/company-statements/gilead-sciences-statement-on-state-attorneys-general-letter-on-remdesivir [https://perma.cc/G6CB-EAHA].

[37]*Id.*

[38]*Id.*

[39]Letter from Senator Warren et. al., to Alex Azar, Secretary, U.S. Dep't of Health & Hum. Servs. (Nov. 16, 2020), https://www.warren.senate.gov/imo/media/doc/2020.11.16.%20Letter%20to%20HHS%20re%20Remdesivir%20Pricing.pdf [https://perma.cc/44B8-6QVT].

[40]*Id.* at 2.

[41]28 U.S.C. § 1498(a) (2011). Reasonable and entire compensation includes "reasonable costs, including reasonable fees for expert witnesses and attorneys, in pursuing the action if the owner is an independent inventor, a nonprofit organization, or an entity that had no more than 500 employees at any time during the 5-year period preceding the use or manufacture of the patented invention." *Id.*

[42]*See* Dan Mangan, *Coronavirus: Federal government will end funding for 13 community-based Covid-19 test sites, most in Texas*, CNBC (June 24, 2020, 1:54 PM), https://www.cnbc.com/2020/06/24/coronavirus-federal-government-to-end-funding-some-covid-19-test-sites.html [https://perma.cc/7LEQ-ZUDR]; *Some COVID-19 Relief Funds Went to Healthcare Cos Under Scrutiny For Possible Fraud, Report Says*, PYMNTS.com (May 3, 2020), https://www.pymnts.com/news/security-and-risk/2020/some-covid-19-relief-funds-went-to-healthcare-cos-under-scrutiny-for-possible-fraud-report-says/ [https://perma.cc/6CE5-DNAN]; Sophie Quinton, *Critic Question CARES ACT Spending in Some States*, PEW (Aug. 7, 2020), https://www.pewtrusts.org/en/research-and-analysis/blogs/stateline/2020/08/07/critics-question-cares-act-spending-in-some-states [https://perma.cc/2ZPZ-3B6H].

questioning the use of significant amounts of taxpayer money to fund research that will ultimately be the subject of a patent, allowing companies to exclude others from access and use of the patented drug and production methods.[43] While scrutiny of the relationship among federal funding, patents, and costs is not new, the urgency of the pandemic and the need for widespread access to lifesaving drugs and vaccines has thrust the issue into the mainstream.[44] Several federal mechanisms are providing COVID-19 funding, including the CARES Act and OWS. The recently enacted CARES Act, totaling $2 trillion, supports the development of vaccines and treatments, including $3.5 billion dedicated to the Biomedical Advancement Research and Development Authority ("BARDA") under HHS.[45]

The implementation of OWS, announced in May 2020, also provides financial incentives to "advance candidate medical countermeasures towards licensure or approval by the U.S. FDA" and "will also serve to advance the knowledge and scientific understanding of candidates' platform technologies, modeling and forecasting, and visual analytics."[46] At the highest level, coordination efforts like OWS, imply rapidity in development and approval tied directly to BARDA funding.[47] OWS engages with "private firms and other federal agencies, including the Department of Agriculture, the Department of Energy, and the Department of Veterans Affairs. It … coordinate[s] existing HHS-wide efforts, including the NIH's Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership, NIH's Rapid Acceleration of Diagnostics (RADx) initiative, and work by BARDA."[48] The three vaccines currently subject to EUAs in the United States, sponsored by Pfizer/BioNTech, Moderna, and Johnson & Johnson, resulted from or benefited from OWS funding or contracts.

A March 2021 report by the Congressional Research Service ("CRS") identifies details of the contracts issued through BARDA and OWS to eight companies: Pfizer/BioNTech, Moderna, AstraZeneca/Oxford University, Johnson & Johnson (Janssen Pharmaceuticals), Novavax, Sanofi/GSK, and Merck/IAVI.[49] Despite $38 million in BARDA support, Merck discontinued clinical trials for its viral vector due to a lack of demonstrated efficacy.[50] Merck has since partnered with Johnson & Johnson to ramp up manufacture of the Johnson & Johnson vaccine that achieved EUA status in February 2021.[51] The CRS

[43] *See* Arthur Allen, *For Billion-Dollar COVID Vaccines, Basic Government-Funded Science Laid the Groundwork*, Scientific American (Nov. 18, 2020), https://www.scientificamerican.com/article/for-billion-dollar-covid-vaccines-basic-government-funded-science-laid-the-groundwork/ [https://perma.cc/T9TQ-WR5A]; Judy Stone, *The People's Vaccine—Moderna's Coronavirus Vaccine Was Largely Funded By Taxpayer Dollars*, Forbes (Dec. 3, 2020, 11:00 AM), https://www.forbes.com/sites/judystone/2020/12/03/the-peoples-vaccine-modernas-coronavirus-vaccine-was-largely-funded-by-taxpayer-dollars/?sh=333f23c46303 [https://perma.cc/2ET5-TCHV].

[44] Press Release, Food Drug Admin., *Emergency Use Authorization for Vaccines Explained*, https://www.fda.gov/vaccines-blood-biologics/vaccines/emergency-use-authorization-vaccines-explained [https://perma.cc/NLM3-SPLP] (last visited April 11, 2021).

[45] H.R. 748, 116th Cong. (2020).

[46] Dep't of Health & Hum. Servs., BAA-18-100-SOL-0003, Office of Biomedical Advanced Research and Development Authority (BARDA) Broad Agency Announcement (BAA) (2021); *Fact Sheet: Explaining Operation Warp Speed*, *supra* note 15.

[47] Fact Sheet: Explaining Operation Warp Speed, *supra* note 15.

[48] *Id.*

[49] Simi V. Siddalingaiah, Cong. Res. Serv., IN11560, Operation Warp Speed Contracts for COVID-19 Vaccines and Ancillary Vaccine Equipment (2021), https://crsreports.congress.gov/product/pdf/IN/IN11560 [https://perma.cc/B9ED-6WWC].

[50] *Id.* at 2.

[51] *Why We're Excited to Partner on Johnson & Johnson's COVID-19 Vaccine,* MERCK (Mar. 10, 2021), https://www.merck.com/stories/why-were-excited-to-partner-on-johnson-and-johnsons-covid-19-vaccine/ [https://perma.cc/2NPC-SBHC].

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report expressly asserts: "Vaccine candidates that received federal government support for development include Moderna, Janssen Pharmaceuticals, Sanofi/GSK, and Merck/IAVI … whereas the Pfizer/BioNTech, Janssen, and Novavax candidates participated in OWS through federal purchase of doses only."[52] This distinction is not without importance, as Pfizer has frequently emphasized that their funding was a contract for the manufactured product rather than the vaccine's basic and clinical research. In a New York Times article, Pfizer's Senior Vice President and head of vaccine research and development is quoted as saying "[w]e were never part of the Warp Speed," and "we have never taken any money from the U.S. government, or from anyone."[53] A spokesperson for Pfizer later clarified that Pfizer was indeed a part of OWS, as a supplier.[54] The CRS report indicates a $5.97 billion contract for 300 million doses of the Pfizer vaccine.[55]

There is increasing concern about what costs will look like post-pandemic, when the international health emergency ebbs and life returns to some semblance of normalcy. Federal funding and contracts are likely conditioned on the presence of the pandemic, with much of the costs for diagnostics, drugs, and vaccines, borne by the government. Once the pandemic subsides, the public will largely be left to pay for approved products out of pocket or through insurance. Media outlets reported in mid-March 2021 that Pfizer's Chief Financial Officer informed shareholders that there was "significant opportunity" to raise the vaccine price in the future when the pandemic becomes endemic.[56] The statement was captured in a conference transcript published on the Pfizer website and immediately drew scrutiny.[57] The projection of the price increase was premised on a return to market prices once the pandemic subsided and the virus was relegated to seasonal booster status. The statement has sparked an active discussion about whether such a move is ethical and whether the government has a responsibility to restrain such industry price-escalating behaviors.[58]

Aside from COVID-19 funding mechanisms, the general connection between federal government funding, licensing practices, and resulting patent protections is under examination by several entities, including the Government Accountability Office ("GAO"). One prominent area of focus is the transparency and reporting elements of these connections. The GAO published an October 2020 report finding that research conducted at HHS laboratories led to approximately 4446 patents between 1980 and 2019, with ninety-three, or only two percent, of those patents owned by the NIH and with the NIH having contributed to the successful development of thirty-four FDA-approved drugs and vaccines.[59] The GAO explored the licensing arrangements associated with these thirty-four drugs and found that the NIH did not have public reporting mechanisms in

[52] Siddalingaiah, *supra* note 49, at 1-2 (depicted in Table 1).

[53] *Was the Pfizer Vaccine Part of the Government's Operation Warp Speed?*, N.Y. Times (Nov. 10, 2020), https://www.nytimes.com/2020/11/10/health/was-the-pfizer-vaccine-part-of-the-governments-operation-warp-speed.html [https://perma.cc/FD5J-6ECQ].

[54] *Id.*

[55] Siddalingaiah, *supra* note 49, at 1-2.

[56] Swikar Oli, *Pfizer Exec Sees 'Significant Opportunity' to Increase COVID Vaccine Price for Annual Booster Shot*, Nat'l Post (Mar. 16, 2021), https://nationalpost.com/news/world/pfizer-exec-sees-significant-opportunity-to-increase-covid-vaccine-price-for-annual-booster-shot [https://perma.cc/9U4U-6JNF].

[57] *Id.*

[58] *See* Emerald Bensadoun, *Pfizer CFO hints at raising COVID-19 vaccine price, but company says "too early" to tell*, Global News (March 17, 2021), https://globalnews.ca/news/7702146/pfizer-covid-vaccine-pricing/ [https://perma.cc/SEN4-J36S].

[59] Government Accountability Office Report to Congressional Requesters, GAO 21-52, Biomedical Research: NIH Should Publicly Report More Information about the Licensing of Its Intellectual Property (2020).

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place, leading to a lack of patent licensing transparency which would assist in evaluating those patents' impact on drug costs and patient access.[60] The GAO recommended that the NIH develop a means to disclose more information to the public about licensing of intellectual property to inform discussions about the effect on public health access and costs.[61]

Recent inquiries into federal funding outcomes are not isolated to vaccine and drug development. Previously, in March 2020, the Office of Science and Technology Policy Subcommittee on Open Science held a public meeting to discuss opportunities to "increase access to unclassified published research, digital scientific data, and code" funded by the federal government.[62] While not pertaining directly to drug development, the meeting signals a similar interest in making publicly available more information about the use of federal money to support commercial research and development.

III. PANDEMIC PATENT RIGHTS AND ENFORCEMENT

Closely tied to research and development are intellectual property protections afforded through patent law. The PTO reviews and issues patents covering compositions, methods, and processes associated with drugs and vaccines.[63] These patents vary in scope, depending on the type of patent and the drafted claims. For example, a patent may assert claims to the chemical composition of the drug compound itself, the delivery system, the mechanism or method of treatment, the manufacturing process, or a combination of the above. The bounds of the patent rights are defined by the precise claim language within the patent.[64] Incremental changes to a patented composition, method, or process are also patent-eligible if those changes satisfy the substantive patent law requirements of utility, novelty, nonobviousness, and an adequate written description of the invention.[65] Once a patent is awarded, the patent holder maintains an exclusive right to that invention for twenty years from the filing date.[66] Federal law also provides for periods of patent term extension to account for the length of the drug approval process.[67]

Pharmaceutical companies are well-known for the protectionist measures they employ to ensure dominance in the market.[68] The pandemic era is no different, in that patents and the scope of patent claims, will play a role in determining cost and access to FDA-approved drugs and vaccines for COVID-19. The PTO is often criticized for issuing patents that are overly broad; subsequent litigation commonly resolves issues with patent claim scope and drafting.[69] In fact, in a Federal Trade Commission ("FTC") report, the agency noted that paragraph IV challenges to litigated patented innovator drug products resulted in victories for the generic company in seventy-three percent of

[60] *Id.*
[61] *Id.*
[62] Office of Science and Technology Policy, Request for Information: Public Access to Peer-Reviewed Scholarly Publications, Data and Code Resulting from Federally Funded Research, 85 Fed. Reg. 9488 (Feb. 19, 2020).
[63] 35 U.S.C. § 2 (2018).
[64] 35 U.S.C. § 112 (2018).
[65] 5 U.S.C. §§ 101, 102, 103, 112 (2019).
[66] 35 U.S.C. § 154 (2019).
[67] 35 U.S.C. § 156 (2019).
[68] *See* Allie Nawrat, *From Evergreening To Thicketing: Exploring The Manipulation Of Pharma Patents*, PHARM. TECH. (Nov. 11, 2019), https://www.pharmaceutical-technology.com/features/pharma-patents-manpulation/ [https://perma.cc/8GBC-4MXT].
[69] *See* David Orozco, *Administrative Patent Levers*, 117 PENN ST. L. REV. 1, 15, 45 (2012).

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cases.[70] Yet, even with resolution of overly broad or invalid patents, a 2018 report available on the FTC website reveals that the twelve top-selling drugs in the United States held, on average, seventy-one patents per drug.[71] And of these twelve top-selling drugs, prices have increased by sixty-eight percent since 2012.[72] The FTC reported in 2009 that the first generic to enter the market typically offers a price twenty-five percent lower than the innovator product, which grows to eighty percent lower cost when multiple generics are on the market.[73] More recent FDA studies reveal that the first generic drug product to enter the market enters at thirty-nine percent lower average manufacturer price ("AMP") than the brand AMP prior to generic competition.[74] With two generic products on the market, AMP is fifty-four percent lower, and the price reductions continue as more generics enter the market.[75] Additionally, the prominence of reverse payments, also known as pay-for-delay settlements, signals that maintaining market dominance for as long as possible ensures lucrative returns.[76] Extensive economics literature details the various impacts patent expiration and market entry of generic drugs have on overall drug costs.

The patent landscape pertaining to the methods, compositions, and processes associated with COVID-19 inventions is dominated by industry. As the New York Times reported in a March 21, 2021 article: "Despite the hefty government funding, drug companies control nearly all of the intellectual property and stand to make fortunes off the vaccines. A critical exception is the patent expected to be approved soon—a government-led discovery for manipulating a key coronavirus protein."[77] The coronavirus patent involves methods of protein manipulation, developed by government scientists studying Middle East Respiratory Syndrome in 2016.[78] In collaboration with scientists at the Scripps Research Institute and Dartmouth College, the NIH filed for a patent, positioned to be issued at the end of March 2021.[79]

In the context of patent protections and impact on costs, several recent actions in the industry patent space during the pandemic deserve special mention. The first is Moderna's October public pledge not to enforce their COVID-related patents "against those making vaccines intended to combat the pandemic" while the pandemic remains a

[70]Fed. Trade Comm'n, Generic Drug Entry Prior to Patent Expiration: An FTC Study (2002) (citing the Congressional Budget Office). A "paragraph IV" certification is where the generic drug sponsor certifies to the FDA that the innovator drug patent is either invalid or unenforceable, ostensibly forcing patent infringement litigation where the innovator wants to assert their patent rights. Food, Drug & Cosmetic Act, Pub. L. No. 116-304, § 505(j)(A)(vii)(IV) (2021); 21 U.S.C. § 355(j)(2)(A)(vii)(IV) (2019).

[71]I-Mak, Overpatented, Overpriced: How Excessive Pharmaceutical Pricing is Extending Monopolies and Driving Up Drug Prices (2018), https://www.ftc.gov/system/files/documents/public_comments/2018/08/ftc-2018-0055-d-0036-155042.pdf [https://perma.cc/JBS6-F8FT].

[72]*Id.* The drugs examined were both chemically synthesized drugs and biological products.

[73]Fed. Trade Comm'n, Emerging Health Care Issues: Follow-On Biologic Drug Competition, at 12 (2009), https://www.ftc.gov/sites/default/files/documents/reports/emerging-health-care-issues-follow-biologic-drug-competition-federal-trade-commission-report/p083901biologicsreport.pdf [https://perma.cc/V2KX-5HLP].

[74]U.S. Food & Drug Admin., Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices, at 2 (2019), https://www.fda.gov/media/133509/download [https://perma.cc/8X8D-ZY5G].

[75]*Id.* at 3.

[76]*See, e.g.*, Michael A. Carrier, *Payment After Actavis*, 100 Iowa L. Rev. 7, 13 (2014).

[77]Selam Gebrekidan & Matt Apuzzo, *Rich Countries Signed Away the Chance to Vaccine the World*, N.Y. Times (Mar. 21, 2021), https://www.nytimes.com/2021/03/21/world/vaccine-patents-us-eu.html [https://perma.cc/4QPS-4RUS].

[78]*Id.*

[79]*Id.*

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public health emergency.[80] Moderna's mRNA vaccine candidate was the second to receive an EUA on December 18, 2020.[81] Both the Pfizer vaccine, which was issued an EUA one week earlier, and the Moderna vaccine utilize mRNA technology. Intellectual property law scholars and practitioners have opined already on the impact of the first mRNA patents and the "long game" that this new class of patents could usher in, given the likely broad nature of future patent claims.[82] Moderna's pledge statement includes a list of U.S. patents relevant to the mRNA-1273 vaccine, but does not specify whether these are the only patents for which Moderna will forego enforcement.[83] Moderna's statement also expresses that the company is willing to license out intellectual property for COVID-19 vaccines to others post-pandemic, upon request.[84] The motivation behind Moderna's pledge is not clear. Some scholars posit that Moderna's research for these patents was partially funded by the NIH, and thus the pledge may dissuade the NIH from pursuing its patent claims aggressively, potentially invalidating some of Moderna's patents.[85] Additionally, Moderna's willingness to license its technology will open the market for it to profit from fees paid from the uptake of its technology, allowing Moderna to continue this line of business post-pandemic, after demand for the vaccine subsides.[86]

Moderna is not the only vaccine manufacturer that has loosened enforcement of intellectual property rights during the pandemic. After governments in Canada, Germany, Israel, Ecuador, and Chile enacted measures to ensure access to pandemic-related technologies through compulsory patent licensing, several other firms began making their technologies freely available on a voluntary basis to fight the pandemic.[87] These pledges come in a variety of forms, including unilateral and coordinated pledges, and for multiple products, including diagnostics equipment, ventilators, and publications.[88] Similar to Moderna's October 2020 pledge, AbbVie declared in March 2020 that it would not enforce its patent rights to the drug Kaletara, which was previously used as an HIV therapy, after Israel explored compulsory licensing as a method to obtain the drug.[89] AbbVie's products have focused more on anti-viral drug development than vaccine efforts.[90]

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[80]Press Release, Moderna, Inc., Statement by Moderna on Intellectual Property Matters During the COVID-19 Pandemic (Oct. 8, 2020), https://investors.modernatx.com/node/10066/pdf [https://perma.cc/37FQ-XJFL] [hereinafter Moderna, Inc., Statement During COVID-19 Pandemic].

[81]Press Release, Food Drug Admin., FDA Takes Additional Action in Fight Against COVID-19 by Issuing Emergency Use Authorization for Second COVID-19 Vaccine (Dec. 2020). *See also* Federal Food, Drug, and Cosmetic Act § 564(c), Pub. L. No. 108-276, 118 Stat. 852 (2004) (codified as amended in 21 U.S.C. § 360bbb-3); U.S. Food & Drug Admin., OMB Control No. 0910-0595, Emergency Use Authorization of Medical Products & Related Authorities: Guidance for Industry & Other Stakeholders (2017).

[82]Dani Kass, *Moderna, Pfizer Playing the Long Game with Novel Vaccine IP*, Law360 (Dec. 1, 2020), https://www.law360.com/health/articles/1331837/moderna-pfizer-playing-the-long-game-with-novel-vaccine-ip?nl_pk=f7c5304d-23a2-4a66-b93c-3b9145e8d004&utm_source=newsletter&utm_medium=email&utm_campaign=health&read_more=1 [https://perma.cc/49LU-YHMT].

[83]*See Program Patents*, Moderna, Inc., https://www.modernatx.com/patents [https://perma.cc/XUF6-AAN9] (last visited Apr. 15, 2021).

[84]Moderna, Inc., Statement During COVID-19 Pandemic, *supra* note 80.

[85]Jorge L. Contreras, *Deconstructing Moderna's COVID-19 Patent Pledge*, Harv. L. Petrie-Flom Center: Bill of Health, (Oct. 21, 2020), https://blog.petrieflom.law.harvard.edu/2020/10/21/moderna-covid19-patent-pledge/ [https://perma.cc/9ZLL-79MQ].

[86]*Id.*

[87]Jorge L. Contreras et al., *Pledging Intellectual Property for COVID-19.* 38 Nat. Biotech. 1146, 1146, 1148 (Oct. 2020), https://doi.org/10.1038/s41587-020-0682-1 [https://perma.cc/Z2KG-FW6V].

[88]*Id.* at 1146-47.

[89]Ed Silverman, *AbbVie Will Allow Generic Copies of Its HIV Pill in Israel After the Government Approved a License*, Stat, (Mar. 20, 2020), https://www.statnews.com/pharmalot/2020/03/20/abbvie-israel-hiv-kaletra-coronavirus-covid19/ [https://perma.cc/689S-QHJ5].

[90]*Research and Discovery Efforts Battling COVID-19 and Beyond*, AbbVie, Inc, https://www.abbvie.com/our-science/covid-19-research-development.html [https://perma.cc/7KWP-G5Y7] (last visited Nov. 23, 2020).

Like AbbVie and Moderna, the University of Oxford, which developed a vaccine in conjunction with AstraZeneca, is allowing open access to its patented developments during the pandemic. Any vaccine developed by Oxford will be licensed.[91] The license will allow non-exclusive, royalty-free rights to the technology only for the duration of the pandemic, as defined by the World Health Organization.[92] Like Moderna, Oxford demonstrates willingness to grant post-pandemic licenses, which are likely to come at a fee, for commercial markets.[93] Oxford's loosened restrictions on the use of its patents extends to vaccines, rapid diagnostics, ventilators, therapeutics, and remote monitoring technology.[94]

Other models include the Rapid Deployment Vaccine Collaborative ("RaDVaC"), a not-for-profit collaboration between scientists associated with multiple institutions created to allow sharing of their collective works under open licenses.[95] RaDVaC is part of the coordinated "Open COVID Pledge," which requires participants to publicly commit to making their intellectual property freely available for the purpose of fighting the pandemic.[96] Under the Open COVID Pledge, while information is freely available for use, there will be a suspension of license for licensees who assert patents for the licensor's products.[97] Several prominent patent holders have joined the Open COVID pledge, offering all patents for use in efforts to fight the pandemic.[98]

These developments are promising, although uncertainty abounds as to the practical implications and lengths of industry pledges and open-source sharing models for COVID-19 products. From an informational perspective, identifying relevant patents covering drug and vaccine products is complex and lacks transparency for competitors as a fundamental matter. Federal law sets out the requirements for FDA product approval and variability exists between new drugs and vaccines, which are biological products. The full intricacies of these differences are outside the scope of this Article, but problems arise in accessing information, as discussed in Part IV. The problems with these mechanisms are the topic of recent FDA public meetings and agency consideration.[99] Among requests for stakeholder input, the FDA sought comments on whether to include patent listings for combination products like drug delivery devices, devices whose use is referenced in approved drug labeling, products with a Risk Evaluation and Mitigation Strategy ("REMS"), and inventions with digital applications such as clinical decision support software.[100]

At a basic level, informational asymmetries between drug and biologic regulation have significant implications for the health care system and for the market entry of subsequent products. For new drugs, the drug sponsor must submit patent information to the FDA and list valid patents, which the FDA will make publicly available in a resource

[91] *Expedited Access for COVID-19 Related IP*, Oxford Univ. Innovation, https://innovation.ox.ac.uk/technologies-available/technology-licensing/expedited-access-covid-19-related-ip/ [https://perma.cc/LX3N-PL44] (last visited Nov. 23, 2020).

[92] *Id.*

[93] *Id.*

[94] *Id.*

[95] *About*, Rapid Deployment Vaccine Collaborative, https://radvac.org/a-homepage-section/ [https://perma.cc/49WM-KD5N] (last visited Nov. 23, 2020).

[96] *Id.*; Gunjan Agarwal & Chipo Jolibois, *IP Risks to Consider When Joining 'Open COVID Pledge,'* Law360 (June 30, 2020), https://www.law360.com/articles/1287364 [https://perma.cc/AN4V-ZVQ8].

[97] Contreras et al., *supra* note 87.

[98] *IPR Pledge Database*, Am. U.C. of L., (Nov. 17, 2020), http://www.pijip.org/non-sdo-patent-commitments/ [https://perma.cc/HK2G-W45H] (IPR database of publicly available statements and commitments made with respect to patents and patent licensing).

[99] FDA Listing of Patent Information in the Orange Book; Establishment of a Public Docket: Request for Comments, 85 Fed. Reg. 33169 (June 1, 2020).

[100] *Id.*

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that generic competitors will consult during the process of submitting applications for their products.[101] On the other hand, biologic sponsors are not required to submit patent information to the FDA as part of the innovator biologic approval process; there is instead a private communication between the follow-on biologic sponsor and the innovator company.[102] The FDA is then required to publish patents identified in that litigation-contemplating private process in a publicly available resource.[103] The next Part delves further into the challenges with patent transparency as related to FDA functioning and resources.

IV. PANDEMIC PATENTS AND INFORMATION DEFICITS

The Federal Food, Drug, and Cosmetic Act ("FDCA") sets forth a special relationship between the FDA and the PTO regarding patents.[104] For the FDA to approve a new drug application ("NDA"), the drug sponsor must submit information to the FDA about any U.S. patents claiming the drug substance, drug product, or method of use.[105] Specifically, the statute requires:

> The applicant *shall file* with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary *shall publish* information submitted under the two preceding sentences.[106]

The FDA publishes this patent information in *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly known as the "Orange Book."[107] Regulations further detail the procedures for submission of patent information.[108] FDA regulations provide that the agency will not accept information about patents unless complete and submitted in the appropriate forms.[109] The FDA also issued a final rule in October 2016 to implement Title XI of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, adding to its patent listing procedure "the date of submission of patents and patent information in the Orange Book."[110] In a frequently asked questions

[101] Federal Food, Drug & Cosmetic Act §505, 21 U.S.C. § 355(b)(1) (2018).

[102] Applications for Biologics Licenses; Procedures for Filing, 21 C.F.R. § 601.2 (2011).

[103] *Purple Book Database of Licensed Biological Products: About Purple Book,* U.S. Food & Drug Admin., https://purplebooksearch.fda.gov/about [https://perma.cc/NHJ3-VPUL] (last visited April 17, 2021).

[104] Federal Food, Drug & Cosmetic Act § 505, 21 U.S.C. § 355 (2018).

[105] *Id.*

[106] *Id.* at § 355(b)(1) (emphasis added).

[107] *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, U.S. Food & Drug Admin., https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm [https://perma.cc/ASM4-9H6R] (last updated April 2021).

[108] 21 C.F.R. § 314.53 (2011); 21 C.F.R. § 314.107 (2002).

[109] 21 C.F.R. § 314.53(c)(1) (2011).

[110] Abbreviated New Drug Applications and 505(b)(2) Applications, 81 Fed. Reg. 69580 (Oct. 6, 2016) (codified in 21 C.F.R. § 314.53(d)(5)).

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document, the FDA provides that patent information must be submitted at the time of the NDA (and certain supplemental applications) on the requisite form and that information regarding subsequent patents must be submitted to the FDA within a specified time-frame.[111] Where a new drug sponsor timely submits the required patent information but is notified that the form is incomplete or the patent is ineligible for listing, the new drug sponsor must submit an acceptable form to be considered timely filed.[112] Holders of an NDA maintain an ongoing obligation to update the accuracy of the drug patent information with the FDA.[113]

Any generic sponsor seeking market entry must consult the Orange Book to assess the patent landscape of the innovator product to craft its abbreviated new drug application ("ANDA").[114] All generic drug sponsors planning to enter the market consult the Orange Book to determine the course of action for their own ANDA. Under the statute, all ANDA applicants, in addition to demonstrating bioequivalence to the innovator NDA drug and fulfilling all other requirements, must expressly address the status of each of the innovator NDA patents and disclose how each patent relates to their drug product and processes.[115] Specifically, a generic drug sponsor intending to enter the market prior to the expiration of existing patents covering the innovator drug must certify for each patent that is listed that it is either invalid, unenforceable, or will not be infringed by the generic product.[116] The certification process serves as a litigation-forcing mechanism, in that the innovator NDA holder will be alerted of the ANDA patent certification by the generic sponsor. The NDA holder can then bring a patent infringement suit against the generic sponsor within forty-five days to determine the legal status of the patent or patents at issue.[117]

An important element of this patent disclosure and publication in the Orange Book is that the FDA views its role as strictly ministerial in function. The Federal Circuit has affirmed this view in *Apotex v. Thompson*, holding that the Hatch-Waxman Act does not require the FDA to review patents substantively prior to listing them in the Orange Book.[118] Both the FDA and SmithKline Beecham Corporation, the NDA holder, contended that the FDA had no duty under the statute to resolve the patent scope and that it was the NDA holder's responsibility to determine whether the patent establishes the drug or method of use for the purpose of required listing.[119] The FDA relied heavily on the language within the statute providing that the NDA holder "shall file" and the FDA "shall

[111]Food, Drug & Cosmetic Act §505(c)(2), 21 U.S.C. § 355(b)(1) (2018); *Frequently Asked Questions on Patents and Exclusivity*, U.S. Food & Drug Admin., https://www.fda.gov/drugs/development-approval-process-drugs/frequently-asked-questions-patents-and-exclusivity [https://perma.cc/6FK8-DW3U] (last updated Feb. 2, 2020).

[112]*Frequently Asked Questions on Patents and Exclusivity*, *supra* note 111.

[113]21 C.F.R. § 314.70(a)(1)(i) (2020).

[114]*See* U.S. Food & Drug Admin., *Patent Certifications and Suitability Petitions* (Apr. 8, 2021), https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/patent-certifications-and-suitability-petitions [https://perma.cc/9ZCP-6LZ4].

[115]Jordan Paradise, *Reassessing 'Safety' for Nanotechnology Combination Products: What Do 'Biosimilars' Add to Regulatory Challenges for the FDA?,* 56 St. Louis U. L. J. 465, 484 (2012).

[116]U.S. Food & Drug Admin., *Patent Certifications and Suitability Petitions*, https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/patent-certifications-and-suitability-petitions#:~:text=To%20seek%20this%20approval%2C%20a%20generic%20applicant%20must,will%20not%20be%20infringed%20by%20the%20generic%20product [https://perma.cc/4GYQ-A7HP] (last updated Dec. 1, 2020).

[117]*Reassessing 'Safety' for Nanotechnology Combination Products: What Do 'Biosimilars' Add to Regulatory Challenges for the FDA?, supra* note 115; Maryll Toufanian & Martin Shimer, *Hatch-Waxman 101*, Regulatory Education for Industry (REdI): Generic Drugs Forum (Apr. 22-23, 2015), https://www.fda.gov/files/drugs/published/Hatch-Waxman-Patent-and-Certification-Process-101.pdf [https://perma.cc/QA93-T2UV].

[118]Apotex, Inc. v. Thompson, 347 F.3d 1335, 1352 (Fed. Cir. 2003).

[119]*Id.* at 1347.

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publish."[120] The Federal Circuit agreed with decisions from the Fourth Circuit, finding that the statute does not clearly speak to the issue of whether Congress intended that the FDA review the substance of patents, and thus deferred to the FDA's reasonable interpretation of the statute.[121]

As noted in the BioX narrative in Part I of this Article, the process for biological products differs from this public database method and consists of a private communication about patent rights once a biosimilar sponsor enters the picture.[122] Before passage of the Biologics Price Competition and Innovation Act ("BPCIA"), there was no abbreviated pathway to market for biological products, and thus subsequent products were typically approved through a full BLA after all relevant patents expired.[123] Given organizational assignments of the agency centers, there were also some products that fell within the biological product definition that were nonetheless approved and regulated as new drugs through the NDA process.[124] For example, insulin has historically been regulated as a drug, but as of March 2020, all insulin products were transitioned into biologics, and all existing NDAs were reclassified as BLAs.[125] Some products regulated as biologics were overseen by the Center for Drug Evaluation and Research rather than the Center for Biologic Evaluation and Research. Prior complexity notwithstanding, and looking prospectively following passage of the BPCIA, the FDA has been busy implementing the new abbreviated pathways to market for biologics, which changed the process by which products entered the market and the requirements for patent disclosure.

Applicants for innovator BLAs are not affirmatively required to file any patent information with the FDA as part of their application. Applicants for subsequent biosimilar products are required to communicate directly with the innovator BLA holder to exchange information about existing patents and the resolution of any potential infringement.[126] The FDA maintains an online *List of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations*, which the agency calls the "Purple Book" database, that lists approved biological products, approval dates, and any licensed biosimilar or interchangeable biological products.[127] Until very recently, the FDA was not required to publish any information about patents in the Purple Book.[128] In pursuing biosimilar status, any subsequent biosimilar competitor must affirmatively provide the innovator biologic sponsor with full information about its biosimilar product application and trust that the innovator will act in good faith in identification and discussion of patent rights and implications for litigation.[129]

Recent legislation makes several changes to this legal landscape. The Consolidated Appropriations Act, 2021 (H.R. 133), containing language of the former Purple

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[120] *Id.*

[121] The relevant interpretation was contained in 21 C.F.R. § 314.53(f) (2020). Apotex, Inc., 347 F.3d at 1351; aaiPharma v. Thompson, 296 F.3d 227, 238 (4th Cir. 2002).

[122] Jordan Paradise, *The Legal and Regulatory Status of Biosimilars: How Product Naming and State Substitution Laws May Impact the United States Healthcare System*, 41 Am. J.L. & Med. 49, 52 (2015).

[123] *Id.* at 50.

[124] *Id.*

[125] *See* Jordan Paradise, *Insulin Federalism*, 27 B.U. J. Sci. & Tech. L. (*forthcoming* 2021).

[126] *See* Paradise, *The Legal and Regulatory Status of Biosimilars: How Product Naming and State Substitution Laws May Impact the United States Healthcare System*, *supra* note 122, at 64.

[127] U.S. Food & Drug Admin., *Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations*, https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/purple-book-lists-licensed-biological-products-reference-product-exclusivity-and-biosimilarity-or [https://perma.cc/8VX4-M74G] (last updated Mar. 5, 2021).

[128] *See* Consolidated Appropriations Act, H.R. 133, 116th Cong. § 325(a)(9)(A)(i)(I) (2021).

[129] 42 U.S.C. § 262(4)(A) (2011).

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Book Continuity Act of 2020 (H.R. 1520), amends the statute to require the FDA to publish in the Purple Book patents of approved biological products identified by the BLA holder during the "patent dance," in a similar format as published in the Orange Book.[130] The patent dance is the process of the confidential, private back-and-forth regarding relevant patents between the innovator biologic and the biosimilar applicant that is set forth in the law.[131] The FDA must also regularly update the Purple Book and identify exclusivity for each biological product.[132] The original Purple Book Continuity Act of 2020 was introduced by Representative Anna G. Eschoo, D-CA, in March 2019, along with ten Democratic and two Republican colleagues.[133] On December 10, 2020, it unanimously passed the Senate and was subsequently incorporated into the Appropriations Act and signed into law on December 27, 2020.[134]

A similar bill, The Orange Book Transparency Act of 2020 (H.R. 1503), introduces several changes to the law for drugs. First, it codifies FDA regulations regarding the listing of drug substance, drug product, and methods of use patents.[135] This language requires that NDA holders provide information for a patent "that claims the drug for which the applicant submitted the application and is a drug substance (active ingredient) patent or a drug product (formulation or composition) patent" or a patent that "claims a method of using such drug for which approval is sought or has been granted in the application."[136] Second, it requires the FDA to specify the exclusivity period for each drug subject to one.[137] Third, it requires that NDA holders notify the FDA when an Orange Book patent is invalidated by a court or the Patent Trial and Appeal Board within fourteen days and that patents found invalid are removed quickly from the Orange Book by the FDA. [138] Finally, it requires the FDA and the Comptroller General to report to Congress on additional types of patents that should or should not be listed in the Orange Book.[139] The Orange Book Transparency Act of 2020 was introduced in March 2019 by Representative Robin Kelly, D-Ill, with one Republican and twelve Democratic co-sponsors. This bill passed the Senate in December and was signed into law on January 5, 2021.

Criticisms of FDA transparency are not limited to patent information and disclosure during product review and approval. The GAO recently published a report on the lack of publicly available information about EUAs[140] during the pandemic as coupled with efforts to speed innovation through OWS.[141] An EUA is not a product approval, but an FDA authorization of the product's use during a public health emergency under expressly

[130]Consolidated Appropriations Act, *supra* note 128. Subtitle C (FDA Amendments), Section 325 contains the Biologic Product Patent Transparency provisions. The "patent dance" is the process of the confidential, private back and forth regarding relevant patents between the innovator biologic and the biosimilar applicant.

[131]42 U.S.C. § 262(l) (2011).

[132]Consolidated Appropriations Act, *supra* note 128 at § 325(a)(9)(A)(iv).

[133]*Id.*

[134]*Id.*

[135]Orange Book Transparency Act of 2020, H.R. 1503, 116th Cong. (2021).

[136]*Id.* at §2(a)(1). The Act also prohibits the submission of patent information outside the scope of the defined categories. *Id.*, at §2(b)(1)(D).

[137]*Id.* at §2(c).

[138]*Id.* at §2(d).

[139]*Id.* at §2(e) & (f).

[140]The FDA published a guidance document for industry in October 2020 providing insight on the process of authorization. U.S. Food & Drug Admin., *Guidance for Industry: Emergency Use Authorizations for Vaccines to Prevent COVID-19* (Feb. 2021), https://www.fda.gov/media/142749/download [https://perma.cc/YYP8-PRM3].

[141]Government Accountability Office, *COVID-19: Federal Efforts Accelerate Vaccine and Therapeutic Development, but More Transparency Needed on Emergency Use Authorizations* (Nov. 17, 2020), https://www.gao.gov/products/GAO-21-207 [https://perma.cc/AM7S-4KWU].

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defined conditions.[142] The GAO report found that the "FDA does not uniformly disclose its scientific review of safety and effectiveness data for EUAs, as it does for approvals for new drugs and biologics."[143] The GAO urged that in the face of the gravity and urgency of the pandemic, the FDA should "identify ways to uniformly disclose this information to the public" to improve both transparency and the public trust.[144]

One incident that may have spurred GAO investigation of the FDA's EUA process is the authorization of convalescent plasma and subsequent misstatements from FDA Commissioner Stephen Hahn. While not directly involving a patent or federally funded research, it does highlight informational transparency issues. During a White House event on August 24, 2020, Commissioner Hahn claimed that a Mayo Clinic trial study of convalescent plasma treatment demonstrated a thirty-five percent reduction in COVID-related deaths.[145] Although it suggested that "transfusion of convalescent plasma with higher antibody levels to hospitalized COVID-19 patients significantly reduc [es] mortality compared to transfusions with low antibody levels," the preliminary paper published by the Mayo Clinic was not yet peer-reviewed and did not substantiate Hahn's claim regarding the steep reduction in mortality resulting from the therapy.[146] Taking the broadest range results in the Mayo study, the treatment would help five out of every hundred patients receiving the plasma, not thirty-five out of one hundred.[147] Hahn corrected his statement in a series of tweets.[148] In granting the EUA for convalescent plasma treatment, the FDA issued a press release, boldly titled: *FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID–19 Treatment, Another Achievement in Administration's Fight Against Pandemic.*[149]

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[142] *See Emergency Use Authorization for Vaccines to Prevent COVID-19*, *supra* note 140 at 3. For an analysis and discussion of the FDA's use of guidance documents during the pandemic, *see* Jordan Paradise & Becky Bavlsik, *Pandemic Politics, Public Health, and the FDA, forthcoming* 8 BELMONT L. REV. (forthcoming 2021).

[143] *Federal Efforts Accelerate Vaccine and Therapeutic Development, but More Transparency Needed on Emergency Use Authorizations*, *supra* note 141.

[144] *Id.*

[145] Associated Press, *Credibility of U.S. Health Agencies At Risk After a Week of Blunders*, LA TIMES (Aug. 28, 2020), https://www.latimes.com/science/story/2020-08-28/credibility-of-u-s-health-agencies-at-risk-after-week-of-blunders [https://web.archive.org/web/20200829033832/https://www.latimes.com/science/story/2020-08-28/credibility-of-u-s-health-agencies-at-risk-after-week-of-blunders].

[146] Michael Joyner et al., *Effect of Convalescent Plasma on Mortality Among Hospitalized Patients with COVID-19: Initial Three- Month Experience* (Aug. 12, 2020) https://www.medrxiv.org/content/10.1101/2020.08.12.20169359v1.full.pdf [https://perma.cc/5PPU-PXW6].

[147] Michael Hiltzik, *Thanks to Trump, the FDA Just Had the Worst Day in its History*, LA TIMES (Aug. 24, 2020), https://www.latimes.com/business/story/2020-08-24/trump-fda-attack-commissioner-stephen-hahn-silent [https://web.archive.org/web/20200824173149/https://www.latimes.com/business/story/2020-08-24/trump-fda-attack-commissioner-stephen-hahn-silent]; Donald Trump, U.S. President, Remarks by President Trump in Press Briefing, Aug. 23, 2020 (Aug. 23, 2020), https://www.whitehouse.gov/briefings-statements/remarks-president-trump-press-briefing-august-23-2020/ [https://web.archive.org/web/20200824054512/https://www.whitehouse.gov/briefings-statements/remarks-president-trump-press-briefing-august-23-2020/].

[148] @SteveFDA, TWITTER (Aug. 24, 2020, 6:36 PM), at https://twitter.com/SteveFDA/status/1298071620414824452 [https://web.archive.org/web/20200825013633/https://twitter.com/SteveFDA/status/1298071620414824452].

[149] *See* U.S. FOOD & DRUG ADMIN., *FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID–19 Treatment, Another Achievement in Administration's Fight Against Pandemic* (Aug. 23, 2020), https://www.fda.gov/news-events/press-announcements/fda-issues-emergency-use-authorization-convalescent-plasma-potential-promising-covid-19-treatment [https://perma.cc/PBJ9-NT9L]; *see also* Associated Press, *Credibility of U.S. Health Agencies At Risk After a Week of Blunders*, LA TIMES, Aug. 28 2020, https://www.latimes.com/science/story/2020-08-28/credibility-of-u-s-health-agencies-at-risk-after-week-of-blunders [https://web.archive.org/web/20200829033832/https://www.latimes.com/science/story/2020-08-28/credibility-of-u-s-health-agencies-at-risk-after-week-of-blunders].

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Another high-profile situation that may have triggered calls for a GAO investigation was the controversy following the FDA's March 2020 EUA issuance for hydroxychloroquine phosphate ("HCQ") and chloroquine phosphate ("CQ") to treat COVID-19.[150] President Trump repeatedly referred to HCQ as a cure for the virus, with little to no scientific evidence to support his claim.[151] On June 15, 2020, the FDA announced that it had revoked the EUAs for HCQ and CQ for the treatment of COVID-19 after determining the two drugs were unlikely to be effective in treating COVID-19 and were causing serious cardiac adverse events and other substantial side effects.[152] Following the GAO report, in November 2020 the FDA has committed to utilize increased transparency mechanisms for EUAs.[153]

V. TOWARD TRANSPARENCY

The COVID-19 pandemic has brought to light significant and systemic informational problems created by the legal and regulatory framework supporting medical innovation. This Article endeavors to highlight the relationship among core regulatory administrative agencies in perpetuating these informational problems across the spectrum of funding, patenting, and product review and approval. Hopefully, the pandemic will result in targeted and wide-ranging introspection about how research is supported in the United States and the way information about the process and the resulting intellectual property rights is made available to the public. These discussions have already begun, at least in connection to how U.S. patent and vaccine nationalism is adversely impacting the rest of the world.[154] This Article does not expressly advocate for the assertion of march-in rights, utilization of compulsory licensing implicating 28 U.S.C. section 1498, or massive statutory or regulatory adjustments to patent law or FDA processes. Instead, this Part offers several modest recommendations to enhance informational transparency that will assist the public, lawmakers, and other stakeholders going forward.

First, there should be continued movement toward uniformity in the online format of the Orange Book and Purple Book as maintained by the FDA. Recent legislation introduces useful changes, though it does not resolve the informational imbalance between

[150] *See* Press Release, U.S. Food & Drug Admin., Coronavirus (COVID-19) Update: Daily Roundup March 30, 2020 (Mar. 30, 2020), https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-daily-roundup-march-30-2020 [https://perma.cc/W2NU-963N].

[151] *See* Elizabeth Y. McCuskey, *FDA in the Time of COVID-19*, 45.3 ADMIN. & REG. L. NEWS 7, 8 (Spring 2020); *see also* Philip Bump, *Trump and Fox Went All-In on a Coronavirus Silver Bullet. But Maybe the Wrong One*, WASHINGTON POST (Apr. 19, 2020), https://www.washingtonpost.com/politics/2020/04/19/trump-fox-went-all-in-coronavirus-cure-what-if-they-picked-wrong-one/ [https://perma.cc/4KSZ-C2V9].

[152] Press Release, U.S. Food & Drug Admin., Coronavirus (COVID-19) Update: FDA Revokes Emergency Use Authorization for Chloroquine and Hydroxychloroquine (June 15, 2020), https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-chloroquine-and#:~:text=Today%2C%20the%20U.S.%20Food%20and,clinical%20trial%20was%20unavailable%2C%20or [https://perma.cc/U6LZ-XT6L].

[153] Press Release, U.S. Food & Drug Admin., COVID-19 Update: FDA's Ongoing Commitment to Transparency for COVID-19 EUAs (Nov. 17, 2020), https://www.fda.gov/news-events/press-announcements/covid-19-update-fdas-ongoing-commitment-transparency-covid-19-euas [https://perma.cc/3LB2-UWY5].

[154] *See, e.g.,* Gebrekidan & Apuzzo, *supra* note 77; DOCTORS WITHOUT BORDERS, *U.S. Must Stop Blocking WTO Waiver on COVID-19 Medical Tools* (Mar. 9, 2021), https://www.doctorswithoutborders.org/what-we-do/news-stories/news/us-must-stop-blocking-wto-waiver-covid-19-medical-tools [https://perma.cc/4MMC-YCXD]; Reuters Staff, *Rich, Developing Nations Wrangle Over COVID Vaccine Patents*, REUTERS (Mar. 10, 2021), https://www.reuters.com/article/us-health-coronavirus-wto/rich-developing-nations-wrangle-over-covid-vaccine-patents-idUSKBN2B21V9 [https://perma.cc/6SYP-S4T6]; Hailey Konnath, *250 Researchers, Orgs Urge WTO to Back COVID IP Waiver*, LAW360 (Mar. 22, 2021), https://www.law360.com/articles/1367374/250-researchers-orgs-urge-wto-to-back-covid-ip-waiver [https://perma.cc/VLZ7-DP65].

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the two resources. The changes also fail to address informational opacity regarding innovator biologic patents, leaving biosimilar sponsors in the dark about the patents that the biologic innovator will assert against them as part of the patent dance. The reference listed BLA holder, the innovator biologic, is required to reveal the select patents identified in the exchange with the biosimilar sponsor to the FDA, which the FDA will then make public in the Purple Book. A subsequent biosimilar sponsor, however, will not be made aware of the full landscape of the innovator biologic's patent rights because those published patents are specific to the exchange with the previous biosimilar sponsor. In the second biosimilar sponsor's patent dance with the innovator biologic, additional patents may be identified as implicated between those two parties. The logical remedy for this problem is to require the innovator biologic to disclose all patents that claim the biologic in the license application. For products already approved, innovator biologics could be required to submit that information to the FDA as well.

Second, the FDA should endeavor to merge the three informationally significant online platforms to the extent possible: the searchable database for drug and biologic approval information (Drugs@FDA),[155] the Orange Book, and the Purple Book. Once merged, users would not have to navigate among the three databases to achieve the complete picture of approval information, labeling information, therapeutic equivalence coding, reference listed products, and patents and exclusivities. Third, and relatedly, Congress should enact legislation that requires the development of an online aggregate database like the NIH's clinicaltrials.gov[156] (reporting information about clinical trials conducted in the United States) or the website usaspending.gov[157] (reporting on COVID-19 related federal spending) to identify and track research funded by the federal government as it pertains to drug, biologic, and medical devices, and eventual health and medical products. Such a website could also utilize hyperlinks to information in the FDA's databases once a product is approved by the FDA. This action would also directly address the concern set forth in the GAO report of NIH reporting of licensing arrangements resulting from the federal funding noted above.[158]

Finally, the PTO and the FDA should consider the creation of a cross-agency body to collaborate on patent issues arising from the interface of the patent approval system and the role that patent information plays in product approval. This entity could identify broad challenges, investigate specific issues that arise, screen and scrutinize patent certification submissions, and study aspects of drug, biologic, and medical device patenting. Other agencies, such as the FTC and the Centers for Medicare and Medicaid Services, might also partner together here to expand study into the impact on costs and access. Likewise, Congress or the Biden Administration could implement such a collaborative through directives, with a range of duties to guide the development of more transparent and user-friendly informational policies and systems.

[155]U.S. Food & Drug Admin., *FDA-Approved Drugs*, Drugs@FDA: FDA-Approved Drugs, https://www.accessdata.fda.gov/scripts/cder/daf/ [https://perma.cc/C7XD-TWM3].

[156]National Insts. of Health, *U.S. National Library of Medicine*, ClinicalTrials.gov [https://perma.cc/L6R7-WCF4].

[157]USA Spending, *Government Spending Open Data*, USAspending.gov [https://perma.cc/9RKA-XNMG].

[158]Government Accountability Office Report to Congressional Requesters, GAO 21-52, Biomedical Research, *supra* note 41.

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