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# Clinical Trial Cost Transparency at the National Institutes of Health: Law and Policy Recommendations

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August 2020





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<b>I.</b>	<b>EXECUTIVE SUMMARY</b>	<b>1</b>
<b>II.</b>	<b>INTRODUCTION</b>	<b>5</b>
<b>III.</b>	<b>THE CASE FOR CLINICAL TRIAL COST TRANSPARENCY AT THE NIH</b>	<b>12</b>
<b>IV.</b>	<b>THE IDEAL: WHAT DATA IS NEEDED</b>	<b>21</b>
<b>V.</b>	<b>EXISTING DISCLOSURE BY THE NIH IS INSUFFICIENT</b>	<b>31</b>
<b>VI.</b>	<b>OPTIONS FOR REFORM AND TOP RECOMMENDATIONS</b>	<b>43</b>
<b>VII.</b>	<b>RESPONSES TO POTENTIAL ARGUMENTS AGAINST R&amp;D COST TRANSPARENCY</b>	<b>56</b>
<b>VIII.</b>	<b>CONCLUSION</b>	<b>61</b>
<b>IX.</b>	<b>ABOUT THE CLINIC, ACKNOWLEDGEMENTS, AND COPYRIGHT NOTICE</b>	<b>64</b>



## I. EXECUTIVE SUMMARY

This report discusses the need for cost transparency into pharmaceutical research and development and, specifically, transparency into the costs of clinical trials funded by the United States National Institutes of Health (NIH), and proposes a set of legislative, administrative, and other reforms to achieve that goal.

**Section II—*Introduction***—provides an overview of current barriers to global access to medicines and how cost transparency into pharmaceutical research and development (R&D) at the NIH and among other drug developers—philanthropic, academic, and industry—can address some of those barriers. Current obstacles to global access to medicines include increasingly high prices charged by pharmaceutical companies and diminishing financial incentives for these companies to develop drugs for diseases that primarily affect small or poor populations. Transparency into four key components of the pharmaceutical market—drug prices, R&D and manufacturing costs, pre-clinical and clinical trial data, and the landscape of patents and other intellectual property—is increasingly being emphasized by advocates as a necessary ingredient in the effort to expand and protect access to affordable, accessible, effective, and safe medicines.

**Section III—*The Case for Clinical Trial Cost Transparency at the NIH***—explains why the policies proposed in this paper target disclosure of disaggregated clinical trial costs at the NIH. Cost transparency into R&D and, particularly, clinical trials, is essential for policymakers to address drug pricing for two reasons: (1) to evaluate the pharmaceutical industry's claims that the high costs of R&D justify the extraordinarily high prices of medicines, and (2) to design policy mechanisms that can incentivize innovation without the monopoly pricing associated with the patent system. This paper focuses on clinical trials in particular because they are often the most expensive aspect of pharmaceutical R&D. Many arguments have been raised against cost transparency into R&D by various stakeholders; though they are worth careful consideration, none of these arguments outweigh the arguments in favor of transparency. This paper focuses on the NIH because it is the largest public funder of biomedical research in the world. As a governmental agency, it spends billions of taxpayer dollars each year, which in itself would justify close oversight by Congress and the public. Transparency into NIH's costs of running clinical trials would provide an important comparison to the cost estimates released by industry-funded studies.

**Section IV—*The Ideal: What Data is Needed?***—presents the list of disaggregated clinical trial cost data points that should be disclosed by the NIH. Existing studies of pharmaceutical R&D costs use undisclosed, self-reported data from pharmaceutical



companies, proprietary databases, or certain publicly available data. None of these are sufficient to present a full picture of clinical trial costs. We discuss an array of potential data points and ultimately propose the following list, based on three considerations: (1) primary drivers of clinical trial costs, (2) administrative ease of collecting and disclosing data, and (3) importance of data points in understanding overall cost.

Costs we recommend should be reported for each study overall, per patient, and per year:

- Personnel costs (including salary and benefits)
  - Administrative staff
  - Clinical staff
- Materials and supplies
- Clinical procedures
- Site management
  - Site monitoring costs
  - Site retention
  - Other
- Central laboratory
- Equipment
- Other direct costs
  - Publication Costs
  - Subawards/Consortium/Contractual Costs
  - Other
- Indirect costs

**Section V—Existing Disclosure by the NIH Is Insufficient**—describes existing ways the NIH shares a limited amount of information with the public and explains the legal sources for that information sharing. Clinical trial sponsors must register applicable trials on ClinicalTrials.gov and submit certain results to the NIH for publication upon trial completion. The NIH is required by statute to administer ClinicalTrials.gov and enforce compliance with the required submissions. Secondly, the NIH maintains RePORTER, a database containing information about NIH research grants, as required by statute. RePORTER records generally include lump-sum grant awards but not disaggregated costs. The NIH also publishes some aggregated data about its research grant awards in the Data Book and certain information about intramural research studies in the intramural database. Lastly, the NIH is required by statute to submit triennial reports to Congress containing certain information, and some institutes and centers within the NIH apparently publish regular reports voluntarily. None of these existing tools accomplishes the clinical trial cost disclosure advocated for in Section IV.



**Section VI—Options for Reform and Top Recommendations**—recommends requiring disclosure on ClinicalTrials.gov of the clinical trial cost data outlined in Section IV. ClinicalTrials.gov is the natural home for specific clinical trial cost data because the website is already structured to collect and display detailed information about each registered trial, and only small changes would be necessary to include cost data. We propose achieving this reform by amending 42 U.S.C. § 282(j), which currently governs ClinicalTrials.gov, in two ways: (1) require that the NIH post the cost data that it possesses for any clinical trial funded in whole or in part by the NIH, and (2) require that all sponsors of clinical trials that receive NIH funding submit the proposed cost data to the NIH to be posted on ClinicalTrials.gov upon study completion. As a next-best or complementary reform, we recommend two improvements to RePORTER: (1) a clearer connection between clinical trials and RePORTER records, and (2) further disaggregating cost information in existing RePORTER records. Congress should amend 42 U.S.C. § 282b, the statute that governs RePORTER, to require these improvements. Lastly, we propose improvements to the Data Book, intramural database, and NIH reports that would help create a clearer picture of clinical trial costs than currently exists, but these improvements are not our main focus, as they would not achieve the reporting goals we lay out in Section IV.

**Section VII—Arguments Against R&D Cost Transparency**—addresses two arguments against reform and concludes that neither should stand in the way of the NIH disclosing this data. The first argument we address is that the administrative burden associated with additional reporting is too high. We believe that cost disclosure will not be especially burdensome because the NIH already requires its grantees to report disaggregated costs, which means grantees already track and the NIH already possesses disaggregated cost data on extramural research. Though we know less about how the NIH tracks its intramural research costs, it is reasonable to expect it to at least do so on the same level it requires of grantees. Finally, the societal benefits of sharing cost information far outweigh potential added costs of reporting. The second argument we address is that cost information on NIH-funded clinical trials is a trade secret or confidential commercial information. Cost data on intramural research conducted exclusively by the NIH, a government agency, cannot be considered a trade secret or confidential commercial information. For extramural grants, HHS and NIH rules, court decisions, and FOIA precedent all agree that clinical trial cost information does not qualify as a trade secret or confidential commercial information and can be disclosed. This suggests that the agency is well within its legal authority to disclose detailed clinical trial cost information. We also address a related argument, primarily raised by industry, that even if it is not legally protected information, disclosure of costs will harm the competitive position of drug developers. We doubt this is the case, because much of this information is already available through publicly disclosed SEC



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filings. As applied to the NIH, we recognize that grantees compete for grants and awards but believe it is fair to require such reporting for researchers who receive public funding.



## II. INTRODUCTION

### A. The State of Global Access to Medicines, Vaccines, and Other Medical Technologies

Around the world, people struggle to get the essential health care they need. A 2017 report from the World Bank and World Health Organization (WHO) concluded that “half the world lacks access to essential health services,” and the costs of health care have pushed almost 100 million people around the world into extreme poverty.<sup>1</sup>

The problem is global. It affects rich countries as well as poor ones. As Doctors Without Borders (Médecins Sans Frontières, MSF) explained in a 2016 report, “[f]ar from being a problem that only affects neglected populations in poorer developing countries, there is now growing recognition that people in wealthier countries are also hit by the shortcomings of the system that drives and finances biomedical innovation today.”<sup>2</sup>

Lack of access to health care is clearly a major concern in the United States. Even before the COVID-19 pandemic of 2020, Americans consistently identified the accessibility and affordability of healthcare as their #1 worry.<sup>3</sup> Health and access to healthcare are near-universal concerns, but the burdens of inadequate health care are not borne equally; access to quality health care is both an indicator and driver of inequality. Within the U.S., there is significant and persistent inequality in health care

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<sup>1</sup> *World Bank and WHO: Half the world lacks access to essential health services, 100 million still pushed into extreme poverty because of health expenses*, World Health Organization (Dec. 13, 2017), <https://www.who.int/news-room/detail/13-12-2017-world-bank-and-who-half-the-world-lacks-access-to-essential-health-services-100-million-still-pushed-into-extreme-poverty-because-of-health-expenses>.

<sup>2</sup> Médecins Sans Frontières (MSF) Access Campaign, *Lives on the Edge: Time to Align Medical Research with People’s Health Needs* 5 (2016) [hereinafter *Lives on the Edge*].

<sup>3</sup> Jeffrey M. Jones, *U.S. Concerns About Healthcare High; Energy, Unemployment Low*, Gallup (Mar. 26, 2018), [https://news.gallup.com/poll/231533/concerns-healthcare-high-energy-unemployment-low.aspx?utm\\_source=alert&utm\\_medium=email&utm\\_content=morelink&utm\\_campaign=syndication](https://news.gallup.com/poll/231533/concerns-healthcare-high-energy-unemployment-low.aspx?utm_source=alert&utm_medium=email&utm_content=morelink&utm_campaign=syndication).



and health outcomes, marked by distressing racial and socioeconomic disparities,<sup>4</sup> which appear to have grown during the COVID-19 crisis.<sup>5</sup>

There are many barriers to universally-accessible, high-quality health care in the U.S. and around the world, but a major one is a lack of access to safe, effective, useful, and affordable medical technologies that people need to live healthy, productive lives: prescription drugs, vaccines, medical devices, diagnostic tests, and so on. Our current system of biomedical discovery, development, and dissemination—by which we mean the political and economic system of public and private entities that invent, develop, validate, license, manufacture, and distribute medical technologies—does not provide adequate access, by numerous measures.<sup>6</sup>

Why is that? In 2016, MSF’s Access Campaign identified<sup>7</sup> four critical ways our current global system of biomedical product discovery, development, and dissemination currently fails to provide people with safe, effective, useful, and affordable medical technologies. We adapt MSF’s “four failings” here, with some additional citations to others’ recent scholarship and commentary:

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<sup>4</sup> See, e.g., Victor R. Fuchs & Karen Eggleston, *Life Expectancy and Inequality in Life Expectancy in the United States*, Stanford Institute for Economic Policy Research (Apr. 2018), <https://siepr.stanford.edu/research/publications/life-expectancy-inequality> (showing increasing inequality in U.S. life expectancy); Shervin Assari, *Why is it so hard to close the racial health gap in the US?*, STAT News (Jan. 9, 2017), <https://www.statnews.com/2017/01/09/racial-health-gap-united-states/> (showing persistent racial disparities in U.S. life expectancy); Laura Dwyer-Lindgren et al., *Inequalities in Life Expectancy Among US Counties, 1980 to 2014*, JAMA INTERNAL MED. (Jul. 2017), <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2626194> (showing geographic disparities in U.S. life expectancy); *When The State Fails: Maternal Mortality & Racial Disparity in Georgia*, Yale Global Health Justice Partnership (2018), [https://law.yale.edu/sites/default/files/area/center/ghjp/documents/ghjp\\_2018\\_when\\_the\\_state\\_fails-\\_maternal\\_mortality\\_racial\\_disparity\\_in\\_georgiarev.pdf](https://law.yale.edu/sites/default/files/area/center/ghjp/documents/ghjp_2018_when_the_state_fails-_maternal_mortality_racial_disparity_in_georgiarev.pdf) (showing wide racial disparities in U.S. maternal mortality).

<sup>5</sup> Aaron van Dorn, Rebecca E Cooney, & Miriam L Sabin, *COVID-19 exacerbating inequalities in the US*, 395 LANCET 10232, 1243-44 (Apr. 18, 2020), [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30893-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30893-X/fulltext); Merlin Chowkwanyun & Adolph L. Reed, Jr., *Racial Health Disparities and Covid-19 — Caution and Context*, N. ENGL. J. MED. (May 6, 2020), <https://www.nejm.org/doi/full/10.1056/NEJMp2012910>.

<sup>6</sup> Margaret Chan, *Ten Years in Public Health 2007-2017*, World Health Organization (2017), <https://apps.who.int/iris/bitstream/handle/10665/255355/9789241512442-eng.pdf;jsessionid=56A812ECA0FB6427CF5B775AB843C39E?sequence=1>; Dana Brown, *Medicine For All: The Case for a Public Option in the Pharmaceutical Industry*, The Next System Project (Sept. 10, 2019), <https://thenextsystem.org/medicineforall>; Ameet Sarpatwari, Dana Brown, & Aaron S. Kesselheim, *Development of a National Public Pharmaceutical Research and Development Institute*, 48 J. LAW MED. & ETHICS 1, 225-27 (Apr. 28, 2020), <https://journals.sagepub.com/doi/abs/10.1177/1073110520917023?journalCode=Imec>.

<sup>7</sup> MSF, *Lives on the Edge*, *supra* note 2 at 5-21.



- (1) **Failing to deliver for diseases that are not sufficiently lucrative.** Our health care system collectively focuses too many resources on discovering, developing, and paying for drugs and other products to treat diseases that afflict wealthy people in wealthy countries, rather than focusing on the diseases that impose the most severe burdens.<sup>8</sup>
- (2) **Failing to prioritize health needs.** Even when our system chooses the right diseases to target, it fails to prioritize products that would best meet pressing health needs—breakthroughs like vaccines and cures—and instead focuses disproportionately on developing “me-too” products that provide only incremental benefits over existing products.<sup>9</sup>
- (3) **Failing to deliver affordable medical products.** The useful drugs, devices, and other medical products that our system does develop are often priced excessively, which makes them inaccessible to many people and overwhelms public and private health care budgets, diverting money that could be spent on other kinds of health care.<sup>10</sup> Excessive prices most

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<sup>8</sup> See Sarah Boseley, *Big pharma failing to invest in new antibiotics, says WHO*, The Guardian (Jan. 17, 2020), <https://www.theguardian.com/business/2020/jan/17/big-pharma-failing-to-invest-in-new-antibiotics-says-who> (failure to develop antibiotics); Paul A. Offit, *Why Are Pharmaceutical Companies Gradually Abandoning Vaccines?*, HEALTH AFFAIRS (May 1, 2005), <https://www.healthaffairs.org/doi/full/10.1377/hlthaff.24.3.622> (long-term decline in vaccine development among major pharmaceutical companies); Jeffrey E. Harris, *Why We Don't Have An HIV Vaccine, And How We Can Develop One*, 28 HEALTH AFFAIRS 6, 1642-54 (2009), <https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.28.6.1642> (failure to develop a vaccine for HIV); Tim Smedley, *Is it fair to accuse the pharma industry of neglecting tropical diseases?*, The Guardian (Oct. 15, 2015), <https://www.theguardian.com/sustainable-business/2015/oct/15/pharma-industry-neglecting-tropical-diseases-snake-bite> (failure to develop treatments for tropical diseases); Dirk Engels & Xiao-Nong Zhou, *Neglected tropical diseases: an effective global response to local poverty-related disease priorities*, 9 INFECT. DIS. POVERTY 10 (Jan. 28, 2020), <https://idpjournal.biomedcentral.com/articles/10.1186/s40249-020-0630-9> (same).

<sup>9</sup> Joshua J. Gagne & Niteesh K. Choudhry, *How Many “Me-Too” Drugs Is Too Many?*, 305 J. AM. MED. ASSOC. 711 (Feb. 16, 2011), [https://jamanetwork.com/journals/jama/fullarticle/645581?casa\\_token=z1RdHDx98skAAAAA:hVBIVnYu8Q10CH3Q7c\\_Ae91jxCpZ-9c6GKJHJffc0Kw9o39dG24QWrsmbwGCUXGeaJ-rYzMybaa](https://jamanetwork.com/journals/jama/fullarticle/645581?casa_token=z1RdHDx98skAAAAA:hVBIVnYu8Q10CH3Q7c_Ae91jxCpZ-9c6GKJHJffc0Kw9o39dG24QWrsmbwGCUXGeaJ-rYzMybaa) (describing overproduction of “me-too” drugs); Q. Claire Xue & Lisa Larrimore Ouellette, *Innovation Policy and the Market for Vaccines*, [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=3595756](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3595756) (describing underproduction of vaccines, cures, and other “durable” medical technologies with long-term effects). “Me too” drugs are “medicines which have only small clinical advantages over existing drugs, but which can be patented and bring substantial profits.” MSF, *Lives on the Edge*, *supra* note 2.

<sup>10</sup> National Academies of Sciences, Engineering, and Medicine, *Making Medicines Affordable: A National Imperative* (Norman R. Augustine, Guru Madhavan, & Sharyl J. Nass, eds., 2018), <https://www.nap.edu/catalog/24946/making-medicines-affordable-a-national-imperative> (describing the drug pricing crisis in the United States); Aaron S. Kesselheim, *Improving competition to lower U.S. prescription drug costs*, Washington Center for Equitable Growth (Feb. 18, 2020), <https://equitablegrowth.org/improving-competition-to-lower-u-s-prescription-drug-costs/> (same); Aaron S. Kesselheim, Jerry Avorn, & Ameet Sarpatwari, *The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform*, 316 J. AM. MED. ASSOC. 8, 858-71 (Aug. 2016), [https://jamanetwork.com/journals/jama/fullarticle/2545691?casa\\_token=bjG\\_sdtRn14AAAAA:QMrrDWO7zua\\_aBTCFW9HM9oM6F\\_FI5rpnV1ug44dLqz9EdNGqThNUmY2oOkEtueeF87iZGshHVuC](https://jamanetwork.com/journals/jama/fullarticle/2545691?casa_token=bjG_sdtRn14AAAAA:QMrrDWO7zua_aBTCFW9HM9oM6F_FI5rpnV1ug44dLqz9EdNGqThNUmY2oOkEtueeF87iZGshHVuC) (same); Toon



commonly arise from an absence of competition and other pricing discipline, caused by intellectual property monopolies<sup>11</sup> (including patents,<sup>12</sup> regulatory exclusivities,<sup>13</sup> and trade secrecy<sup>14</sup>), antitrust violations,<sup>15</sup> and (at least in the U.S.) a lack of pricing negotiation power on the part of public payers.<sup>16</sup>

- (4) **Failing to use scientific and financial resources efficiently and effectively.** Discovery, development, manufacturing, and distribution of medical technologies is slow, inefficient, and often ineffective, due to a lack of data sharing,<sup>17</sup> unnecessary redundancy in R&D, and increasing financialization and underinvestment in the biomedical sector as a whole.<sup>18</sup>

Remaking the global system to address all of these failings is vital, complex, and beyond the scope of this white paper. This paper focuses instead on just one important area where relatively simple changes to law, policy, and practice could go some way toward fixing our broken system: transparency into our global system of research, development, and distribution of medical products. As we show in the next section, expanding transparency would yield considerable benefits—reducing expenditures, accelerating the march of science, and improving clinical care—at relatively little cost.

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van der Gronde, Carin A. Uyl-de Groot & Toine Pieters, *Addressing the challenge of high-priced prescription drugs in the era of precision medicine: A systematic review of drug life cycles, therapeutic drug markets and regulatory frameworks*, PLOS ONE (Aug. 16, 2017), <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0182613> (pricing crisis in the U.S. and Europe).

<sup>11</sup> Robin Feldman, *May your drug price be evergreen*, 5 J. L. & BIOSCIENCES 590 (Dec. 7, 2018), <https://academic.oup.com/jlb/article/5/3/590/5232981>.

<sup>12</sup> *Overpatented, Overpriced: How Excessive Pharmaceutical Patenting Is Extending Monopolies and Driving Up Drug Prices*, I-MAK (2018), <https://www.i-mak.org/overpatented-overpriced-excessive-pharmaceutical-patenting-extending-monopolies-driving-drug-prices/>.

<sup>13</sup> Michael G. Daniel, et al., *The Orphan Drug Act: Restoring the Mission to Rare Diseases*, 39 AM. J. CLINICAL ONCOLOGY 210 (Apr. 2016), <https://insights.ovid.com/article/00000421-201604000-00017>.

<sup>14</sup> Yaniv Heled, *The Case for Disclosure of Biologics Manufacturing Information*, 47 J. L., MED., & ETHICS 54 (Jan. 19, 2020), <https://journals.sagepub.com/doi/abs/10.1177/1073110519898043>.

<sup>15</sup> Michael A. Carrier, *Higher Drug Price From Anticompetitive Conduct: Three Case Studies*, 39 J. LEG. MED. 151 (Sept. 10, 2019), <https://www.ncbi.nlm.nih.gov/pubmed/31503532>.

<sup>16</sup> Juliette Cubanski, Tricia Neuman, Sarah True, and Meredith Freed, *What's the Latest on Medicare Drug Price Negotiations?*, KFF (Oct. 17, 2019), <https://www.kff.org/medicare/issue-brief/whats-the-latest-on-medicare-drug-price-negotiations/>.

<sup>17</sup> *Promoting Transparency in Clinical Research: Why and How*, Collaboration for Research Integrity & Transparency (CRIT) at Yale University (Nov. 2017), [https://law.yale.edu/sites/default/files/area/center/crit/crit\\_white\\_paper\\_november\\_2017\\_best\\_promoting\\_transparency\\_in\\_clinical\\_research\\_why\\_and\\_how.pdf](https://law.yale.edu/sites/default/files/area/center/crit/crit_white_paper_november_2017_best_promoting_transparency_in_clinical_research_why_and_how.pdf).

<sup>18</sup> Mariana Mazzucato, *Rethinking value in health innovation: from mystifications towards prescriptions*, 22 J. ECON. & POL. REFORM 101 (2019), <https://www.tandfonline.com/doi/full/10.1080/17487870.2018.1509712>.



## B. The Role of Transparency in Increasing Access to Medicines and Other Medical Products

Transparency—broad, ready, equitable access to knowledge and to the underlying data that generates that knowledge—is a necessary component of a healthy biomedical innovation system. Transparency promises to accelerate innovation and competition, help focus R&D activity where health needs are most severe and therapeutic benefits are greatest, bring down manufacturing costs and expand supplies, and reduce unnecessary spending by consumers, government, and manufacturers on drugs and other medical technologies, including those technologies that provide few or no real therapeutic benefits.

In February 2019, Italy submitted a draft resolution to the World Health Assembly (WHA) of the WHO entitled, “Improving the transparency of markets for drugs, vaccines and other health-related technologies.”<sup>19</sup> The resolution urged member states of the WHO to create laws and policies that expand and protect transparency into various components of the biomedical innovation system. Here we highlight four key components featured in Italy’s draft resolution<sup>20</sup>:

- (1) **Price Data:** The prices paid by various buyers and distributors of drugs and other medical products.
- (2) **Research Data:** The data generated from clinical research, including the results of clinical trials.
- (3) **R&D Cost Data:** The dollar amount spent on clinical research, and all sources of funding (private, public, and philanthropic), through all means (direct expenditures, tax credits).

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<sup>19</sup> *Improving the Transparency of Markets for Drugs, Vaccines and Other Health-Related Technologies*, World Health Organization (2019), [http://www.salute.gov.it/imgs/C\\_17\\_notizie\\_3670\\_listaFile\\_itemName\\_1\\_file.pdf](http://www.salute.gov.it/imgs/C_17_notizie_3670_listaFile_itemName_1_file.pdf). A later revision of the resolution is available here: *Improving the transparency of markets for medicines, vaccines, and other health related products and other technologies to be discussed at the 72nd session of the WHA to be held on 20-28 May 2019*, World Health Association (May 20, 2019), [https://www.keionline.org/wp-content/uploads/WHA-Resolution\\_DRAFT\\_20-05-2019.pdf](https://www.keionline.org/wp-content/uploads/WHA-Resolution_DRAFT_20-05-2019.pdf).

<sup>20</sup> These are not the only components of the biomedical innovation system into which Italy’s draft resolution called for increased transparency. The draft resolution also called, *inter alia*, for transparency into manufacturing costs, marketing costs, and quantities of medical products sold. *Improving the Transparency of Markets for Drugs, Vaccines and Other Health-Related Technologies*, World Health Organization (2019), [http://www.salute.gov.it/imgs/C\\_17\\_notizie\\_3670\\_listaFile\\_itemName\\_1\\_file.pdf](http://www.salute.gov.it/imgs/C_17_notizie_3670_listaFile_itemName_1_file.pdf). Nor are these four components the only ones wherein greater transparency would be beneficial. See, e.g., CenterWatch Staff, *Does industry need a preclinical database? Robert Califf says yes*, (Jun. 20, 2016), <https://www.centerwatch.com/articles/15022> (then-FDA Commissioner Robert Califf calling for greater sharing of preclinical as well as clinical data); Christopher J. Morten, Amy Kapczynski, Harlan M. Krumholz and Joseph S. Ross, *To Help Develop The Safest, Most Effective Coronavirus Tests, Treatments, And Vaccines, Ensure Public Access To Clinical Research Data*, HEALTH AFFAIRS (Mar. 26, 2020), <https://www.healthaffairs.org/doi/10.1377/hblog20200326.869114/full/> (same).



**(4) Patent and Other Intellectual Property Data:** The patents, trade secrets, and other intellectual property rights that provide certain parties with exclusive rights over drugs and other medical products.

Italy's original resolution was not approved by the WHA because of pressure from a limited number of countries, including Canada,<sup>21</sup> the United Kingdom, Germany, and Hungary.<sup>22</sup> A reduced version of the resolution was ultimately approved, despite support for the original, more robust version by a majority of countries at the WHA.<sup>23</sup> The approved resolution encouraged member states to embrace greater transparency, especially on price data, but imposed no mandatory obligations to do so.<sup>24</sup>

In the lead-up to the WHA resolution, and in the months since, many legislators, policy makers, and civil society groups have called on industry and governments around the world to commit to one or more of these components and begin to complete the unfinished work of the WHA.<sup>25</sup> These calls have been renewed in the COVID-19 pandemic and have become more urgent than ever.<sup>26</sup>

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<sup>21</sup> Kelly Crowe, 'You disappointed us': Why is Canada opposing more transparency in drug prices?, CBC News (May 25, 2019), <https://www.cbc.ca/news/health/who-high-drug-prices-secrecy-transparency-clinical-trial-costs-canada-transparency-resolution-1.5148401>.

<sup>22</sup> Lucy Lamble, UK refuses to back 'game-changing' resolution on drug pricing, The Guardian (May 28, 2019), <https://www.theguardian.com/global-development/2019/may/28/uk-refuses-to-back-game-changing-resolution-on-drug-pricing>.

<sup>23</sup> James Love, KEI Statement on Adoption of the WHA72 Transparency Resolution, Knowledge Economy International (May 28, 2019), <https://www.keionline.org/30887>.

<sup>24</sup> Member States adopt the resolution on 'Improving the transparency of markets for medicines, vaccines, and other health products' at WHA today, MSF Press Release (May 28, 2019), <https://msfaccess.org/member-states-adopt-resolution-improving-transparency-markets-medicines-vaccines-and-other-health>.

<sup>25</sup> See, e.g., MSF, *Lives on the Edge*, supra note 2 (calling for sharing of data on R&D costs and the results of clinical trials); Joshua M. Sharfstein et al., *Blueprint for Transparency at the U.S. Food and Drug Administration: Recommendations to Advance the Development of Safe and Effective Medical Products*, J. L. MED. & ETHICS (2018) (calling for increased transparency into the results of clinical trials and other data held by the U.S. Food & Drug Administration); Ameet Sarpatwari, Rachel Barenie, Gregory Curfman, Jonathan J. Darrow, Aaron S. Kesselheim, *The US Biosimilar Market: Stunted Growth and Possible Reforms*, CLINICAL PHARMACOLOGY & THERAPEUTICS (Vol. 105, Issue 1, Jan. 2019), <https://ascpt-onlinelibrary-wiley-com.proxy.library.nyu.edu/doi/10.1002/cpt.1285> (calling for increased transparency of clinical trial results, patent data, manufacturing data currently held as trade secrets); Steven Findlay, *States Pass Record Number Of Laws To Reel In Drug Prices*, Kaiser Health News (Sep. 9, 2019), <https://khn.org/news/states-pass-record-number-of-laws-to-reel-in-drug-prices/> (summarizing legislation in U.S. states to increase transparency in the prices paid for drugs and other medical technologies).

<sup>26</sup> See, e.g., *Urgent steps are needed to define how COVID-19 medical tools can really be "global public goods"*, MSF (May 20, 2020), <https://msfaccess.org/urgent-steps-are-needed-define-how-covid-19-medical-tools-can-really-be-global-public-goods> (MSF statement of May 1, 2020, calling for "transparency across the board" in the COVID-19 response, including sharing of "the costs and prices at all stages of development, production and distribution" and "[t]echnologies, data and know-how").



The United States has an opportunity to lead on all four key components of transparency highlighted above. For example, the U.S. is home to most of the largest pharmaceutical and biotech companies,<sup>27</sup> publicly funds more biomedical research than any other nation,<sup>28</sup> and spends far more than any nation on purchases of drugs and other medical products.<sup>29</sup> Legislators and policymakers in the U.S. are therefore uniquely positioned to promote—or demand—greater transparency, and, given Americans’ unequaled use of and spending on medical products, no country has more to gain from increased transparency than the U.S.

In some respects, the U.S. is already a leader in transparency. For example, a U.S. federal law mandates significant transparency into some types of research data. In 2007, the U.S. enacted the Food and Drug Administration (FDA) Amendments Act (FDAAA), which requires the trial sponsors of essentially all Phase 2, Phase 3, and Phase 4 clinical trials of all drugs and medical devices (including vaccines and diagnostic tests) to register their trials and report trial results in a publicly accessible internet database, ClinicalTrials.gov, run by NIH.<sup>30</sup> While sponsors’ compliance with registration and results reporting requirements is imperfect, due to inadequate enforcement by FDA and NIH,<sup>31</sup> ClinicalTrials.gov is nonetheless a qualified success and is now the world’s largest publicly accessible database of clinical trial data.<sup>32</sup>

But in other ways, the U.S. lags. For example, while U.S. law mandates public registration and results sharing for most clinical trials, it currently permits drug and

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<sup>27</sup> Monique Ellis, *Who are the top 10 pharmaceutical companies in the world? (2019)*, Proclinical (Mar. 20, 2019), <https://www.proclinical.com/blogs/2019-3/the-top-10-pharmaceutical-companies-in-the-world-2019>.

<sup>28</sup> See Lazonick, William and Tulum, Öner, *US Biopharmaceutical Finance and the Sustainability of the Biotech Business Model*, RESEARCH POLICY, Vol. 40, No. 11, 2011, at 8 (Nov. 1, 2011) (“Through the NIH, the US government, and by extension the US taxpayer, has long been the nation’s (and the world’s) most important investor in knowledge creation in the medical fields.”), <https://ssrn.com/abstract=2257932> or <http://dx.doi.org/10.2139/ssrn.2257932>.

<sup>29</sup> *Pharmaceutical spending*, Organisation for Economic Co-operation and Development (undated), <https://data.oecd.org/healthres/pharmaceutical-spending.htm>.

<sup>30</sup> *FDAAA 801 and the Final Rule*, ClinicalTrials.gov (Aug. 2019), <https://clinicaltrials.gov/ct2/manage-recs/fdaaa>.

<sup>31</sup> Deborah A. Zarin, Kevin M. Fain, Heather D. Dobbins, Tony Tse, and Rebecca J. Williams, *Special Report : 10-Year Update on Study Results Submitted to ClinicalTrials.gov*, N. ENGL. J. MED. 381; 20, (Nov. 14, 2019), <https://www.nejm.org/doi/pdf/10.1056/NEJMsr1907644>; Charles Piller, *FDA and NIH let clinical trial sponsors keep results secret and break the law*, SCIENCE (Jan. 13, 2020), <https://www.sciencemag.org/news/2020/01/fda-and-nih-let-clinical-trial-sponsors-keep-results-secret-and-break-law>; Nicholas J DeVito, Seb Bacon, Ben Goldacre, *Compliance with legal requirement to report clinical trial results on ClinicalTrials.gov: a cohort study*, LANCET (Jan. 17, 2020), [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(19\)33220-9/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)33220-9/fulltext).

<sup>32</sup> Asba Tasneem, Laura Aberle, Hari Ananth, Swati Chakraborty, Karen Chiswell, Brian J. McCourt, and Ricardo Pietrobon, *The Database for Aggregate Analysis of ClinicalTrials.gov (AACT) and Subsequent Regrouping by Clinical Specialty*, 7(3) PLOS ONE (Mar. 16, 2012), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3306288/>.



device manufacturers, universities, federal labs, and other sponsors of clinical trials to keep the costs of those clinical trials secret. This state of affairs is unsatisfactory, but meaningful clinical trial cost transparency can be achieved. As we explain in the following section, a small investment in expanding sharing of clinical trial cost data would produce large social benefits—increased efficiency in medical research, reduced spending on medical products, and (ultimately, through accelerated R&D and better access) improved clinical care. While Congressional action would be ideal, the President and/or NIH can and should act even without statutory amendment to make the NIH a global leader on clinical trial cost transparency, as we explain below.

### III. THE CASE FOR CLINICAL TRIAL COST TRANSPARENCY AT THE NIH

#### A. The Important Role of R&D Cost Transparency in Increasing Access to Medicines and Other Medical Products

Time and again, pharmaceutical companies use the high cost of research and development to justify high drug prices.<sup>33</sup> It is natural, in response, to ask for the numbers. As Representative Jan Schakowsky notes, “drug companies tell us all the time, ‘It’s about R&D; it costs *so much*. . . .’ If you’re going to use that as an excuse for raising prices, we have the absolute right to know how much is being spent.”<sup>34</sup>

In fact, there have been numerous legislative proposals to mandate R&D cost disclosures. For example, in 2015, Senator Bernie Sanders and Representative Elijah Cummings introduced legislation that would require manufacturers of all FDA-approved drugs to submit yearly reports to the Department of Health and Human Services disclosing their total expenditures on R&D, including clinical trials, materials and manufacturing, and other expenses.<sup>35</sup> More moderate proposals that would require

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<sup>33</sup> Robert D. Atkinson, *How the Biopharmaceutical Industry Contributes to Open Scientific Knowledge*, Information Technology & Innovation Foundation (Nov. 2018), [http://www2.itif.org/2018-biopharmaceutical-open-knowledge.pdf?\\_ga=2.100530070.961923108.1592327010-645292166.1591967991](http://www2.itif.org/2018-biopharmaceutical-open-knowledge.pdf?_ga=2.100530070.961923108.1592327010-645292166.1591967991) (claiming an upper limit of \$3.2 billion to bring a drug to market). We are skeptical of the claim that pricing is based on R&D costs, rather than based on what the market will bear. Rather, high R&D costs are a justification used by pharmaceutical companies for high and rising prices. As Ed Silverman at STAT has reported, Ron Cohen, the chief executive of Acorda Therapeutics, stated that with respect to demands for cost transparency, “It is absolutely right that, because we made an argument, society is coming back now and very rightfully holding us to account for the argument . . . It was always the wrong argument . . . But we made our own bed and people are asking us to lie in it.” *With drug costs rising, pharma should open its books*, STAT News (Feb. 16, 2016), <https://www.statnews.com/pharmalot/2016/02/16/drug-cost-transparency/>.

<sup>34</sup> Joyce Frieden, *Transparency Bills May Have Unintended Consequences--Lawmakers hear concerns about provisions on drug samples, price increases*, MedPage Today (May 21, 2019), [cached], <https://www.healthleadersmedia.com/strategy/transparency-bills-may-have-unintended-consequences>.

<sup>35</sup> Prescription Drug Affordability Act, H.R. 3513, 114<sup>th</sup> Cong. § 601(a) (2015); Prescription Drug Affordability Act, S. 2023, 114<sup>th</sup> Cong. § 601(a) (2015).



industry to justify price increases above a certain threshold, including disclosure of R&D costs, have achieved bipartisan support in Congress, but none have been passed into law.<sup>36</sup> Additionally, states such as California and Oregon have enacted state legislation to require industry to justify certain price increases, including disclosure of R&D costs, at the risk of monetary penalties.<sup>37</sup>

The reality is, despite many attempts to quantify actual R&D costs over the last several decades,<sup>38</sup> costs remain opaque. Not only are there a wide range of estimates on the cost to produce new treatments, vaccines, diagnostics, and other medical tools, but, as the National Academy of Medicines pointed out in their 2018 report *Making Medicines Affordable*, “questions abound regarding the reliability of these studies and their estimates.”<sup>39</sup> Legislators and policymakers on both sides of the aisle have sought more information on R&D costs to better understand pharmaceutical pricing—and been unable to get it. For example, in a letter from U.S. Senators Ron Wyden and Charles Grassley to Gilead on the pricing of Sovaldi, a breakthrough treatment for Hepatitis C, the Senators requested records of “itemized accounting” of research and development costs.<sup>40</sup> Gilead declined to provide the development cost data to Senators Wyden and Grassley; their staffs later wrote that “despite the company’s assurances of cooperation, Gilead failed to produce all relevant documents and supporting materials related to pricing,”<sup>41</sup> including “how much additional cost it incurred to complete the development” of Sovaldi.

There are reasons to disbelieve the narrative that high R&D costs are what drive high prices. Gilead’s pricing of Sovaldi again proves a useful example. The majority of R&D associated with Sovaldi was conducted by a pharmaceutical company called Pharmasset, which was purchased by Gilead before Sovaldi was brought to market. Prior to its purchase by Gilead, Pharmasset “expected to profitably sell the drug in the

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<sup>36</sup> See, e.g., Fair Accountability and Innovative Research Drug Pricing Act, H.R. 2439, 115<sup>th</sup> Cong. § 39900(c) (2017) (led by Rep. Schakowsky [D-IL-9] and co-sponsored by Reps. Francis Rooney [R-FL-19] and Peter King [R-NY-2]); Fair Accountability and Innovative Research Drug Pricing Act, S. 1131, 115<sup>th</sup> Cong. § 39900(c) (2017) (sponsored by Sen. Tammy Baldwin [D-WI] and co-sponsored by Sen. John McCain [R-AZ]).

<sup>37</sup> S-B 17, 2017-18 Reg. Sess. (Ca. 2017); H.B. 4005, 79<sup>th</sup> Leg. Assembly, Reg. Sess. (Or. 2018).

<sup>38</sup> See Section IV for more discussion on previous estimates of R&D costs.

<sup>39</sup> National Academies of Sciences, Engineering, and Medicine, *Making Medicines Affordable*, 88 (2018), <https://doi.org/10.17226/24946>.

<sup>40</sup> Ron Wyden & Charles E. Grassley, *Senators Seek Details on Sovaldi Pricing*, News Release (Jul. 11, 2014), <https://www.grassley.senate.gov/news/news-releases/senators-seek-details-sovaldi-pricing>.

<sup>41</sup> *The Price of Sovaldi and Its Impact on the U.S. Health Care System*, Committee on Finance, U.S. Senate, (Dec. 2015), [https://www.finance.senate.gov/imo/media/doc/1%20The%20Price%20of%20Sovaldi%20and%20Its%20mpact%20on%20the%20U.S.%20Health%20Care%20System%20\(Full%20Report\).pdf](https://www.finance.senate.gov/imo/media/doc/1%20The%20Price%20of%20Sovaldi%20and%20Its%20mpact%20on%20the%20U.S.%20Health%20Care%20System%20(Full%20Report).pdf).



United States for \$36,000” for a standard treatment; after acquiring Pharmasset, Gilead set the price of Sovaldi at \$84,000 for a standard treatment.<sup>42</sup>

Furthermore, recent studies show that prices in the U.S. “generate[] substantially more than the companies spend globally on their research and development”<sup>43</sup> and that revenues on ten cancer drugs are “substantially higher than the preapproval research and development spending.”<sup>44</sup> Critics of this high-cost, high-price narrative point to the high profit margins of pharmaceutical companies and the amount these companies spend on marketing.<sup>45</sup> At the same time that pharmaceutical companies cite high costs of R&D to justify high prices of medicines, their trade organizations have also stated: “We also caution against disclosure requirements on R&D costs that underscore ‘cost-plus’ models. Prices should reflect the therapeutic value of medicines and positive outcomes for patients and society, rather than simply the cost ‘input’ of an individual medicine.”<sup>46</sup> Therefore, there is reason to believe that while industry sometimes uses high costs of R&D to defend their pricing practices, medicines are not actually priced based on the cost of development. If that is the case, disclosure of clinical trial costs will expose that industry does not in fact set prices based on the costs it so frequently cites.

Transparency into R&D costs is thus important to challenge the high drug and device prices that result in lack of access. Though it is well-accepted in the access to medicines community that drug prices and profits earned by pharmaceutical companies are far higher than necessary to recoup R&D costs,<sup>47</sup> the same is not necessarily true of legislators, policymakers, and the general public. To achieve comprehensive pricing reform, advocates need to prove to members of Congress, other government actors,

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<sup>42</sup> *Id.*

<sup>43</sup> Nancy L. Yu, Zachary Helms, Peter B. Bach, *R&D Costs For Pharmaceutical Companies Do Not Explain Elevated US Drug Prices*, HEALTH AFFAIRS (Mar. 7, 2017), <https://www.healthaffairs.org/doi/10.1377/hblog20170307.059036/full/>.

<sup>44</sup> Vinay Prasad & Sham Mailankody, *Research and Development Spending to Bring a Single Cancer Drug to Market and Revenues After Approval*, 177 JAMA INTERNAL MED. 1569, 1570 (2017), <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2653012>.

<sup>45</sup> See Ezekiel J. Emanuel, *Big Pharma’s Go-To Defense of Soaring Drug Prices Doesn’t Add Up*, THE ATLANTIC (Mar. 23, 2019) <https://www.theatlantic.com/health/archive/2019/03/drug-prices-high-cost-research-and-development/585253/>.

<sup>46</sup> IFPMA Statement on Access to Medicines, Agenda Item 11.7 WHA 72 (May 2019), [https://www.ifpma.org/wp-content/uploads/2019/05/IFPMA\\_Statement\\_ATM\\_WHA72\\_FINAL.pdf](https://www.ifpma.org/wp-content/uploads/2019/05/IFPMA_Statement_ATM_WHA72_FINAL.pdf).

<sup>47</sup> Christine Ro, *No One Knows The True Cost Of Medicines, And Blaming Other Countries Won't Help*, FORBES (Mar. 3, 2019), <https://www.forbes.com/sites/christinero/2019/03/03/no-one-knows-the-true-cost-of-medicines-and-blaming-other-countries-wont-help/#7c109f045ce5> (“It’s a myth that the costs of medicines need to be high, to cover the research & development costs of pharmaceutical companies. Research shows that profits are much higher than necessary to justify past and future R&D, the pharma industry has one of the highest profit margins around, and the industry spends almost twice as much on marketing as on R&D. ... Prices in the pharma industry aren’t set based on a particular acceptable level of profit, or in relation to the cost of production.”).



and the public who vote for them that R&D costs do not justify high medicine prices. Armed with true R&D costs, legislators and policymakers can design better law and policy to facilitate necessary medical product development while still ensuring those products are affordable and accessible.<sup>48</sup> Additionally, armed with more information regarding the costs to develop a particular drug, buyers—including patients and other payers, public and private—will have a better negotiating position.<sup>49</sup>

Reliable R&D costs will be particularly important not only to pursue incremental changes to existing incentive mechanisms, but also to advocate for systemic change in the pharmaceutical industry. For instance, some groups advocate nationalizing pharmaceutical research and development,<sup>50</sup> while others advocate “break[ing] the link that today binds biomedical innovation to drug sales and exclusivity rights.”<sup>51</sup> These proposals typically rely on expanded public-sector R&D and/or new incentive mechanisms such as publicly-funded prizes, all of which must be designed based on the actual costs of research and development.<sup>52</sup> For example, in order for a prize system to work, the prize-setter must understand the dollar amount necessary to incentivize firms to compete; if it is too low, the goals will not be accomplished, but if it is too high, the public still overpays for the drug. Knowledge of the true cost of clinical trials will help governments both fund their own clinical trials and offer appropriate incentives for others to complete clinical trials.<sup>53</sup>

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<sup>48</sup> James Love, *BIO memo opposing transparency of drug development costs, sales, prices and clinical trial outcomes*, Knowledge Economy International (May 21, 2012), <https://www.keionline.org/21844> (“[D]oes anyone in the Congress actually know what the private sector spends on clinical trials for AIDS drug development? Do they know how much it costs for the trials that justify the pediatric marketing exclusivity? Can they explain what it costs to get an orphan drug designation, or what the impact of the designation is on the prices of an older generic drug that is suddenly re-classified as a monopoly? And, if not, is this ignorance really appropriate for a legislative body?”); see also *Legislative Guide for Insulin for All: How States Can Make Medicines Affordable*, Public Citizen and T1International USA (May 2020), [https://www.t1international.com/media/assets/file/Public\\_Citizen\\_T1International\\_Insulin\\_for\\_All\\_Legislative\\_Guide\\_-\\_May\\_2020.pdf](https://www.t1international.com/media/assets/file/Public_Citizen_T1International_Insulin_for_All_Legislative_Guide_-_May_2020.pdf) (recommending that state governments require transparency into “research and development costs, marketing expenses, pricing strategies and profits” to support laws and policies that expand access to affordable insulin).

<sup>49</sup> MSF briefing on provisional agenda item 11.7 of 72nd WHO World Health Assembly – May 2019, *Access to medicines and vaccines, Draft resolution on improving the transparency of markets for medicines, vaccines, and other health-related technologies*, 3, [https://msfaccess.org/sites/default/files/2019-05/WHO-WHA-72\\_MSFBriefingTransparencyAgendaItem-11-7.pdf](https://msfaccess.org/sites/default/files/2019-05/WHO-WHA-72_MSFBriefingTransparencyAgendaItem-11-7.pdf).

<sup>50</sup> Dana Brown & Ameet Sarpatwari, *A National Pharmaceutical Research and Development Institute*, The Next System Project (Nov. 4, 2019), <https://thenextsystem.org/learn/stories/national-pharmaceutical-research-and-development-institute>.

<sup>51</sup> MSF, *Lives on the Edge*, *supra* note 2 at 4.

<sup>52</sup> Love, *supra* note 48 (“S. 1138 proposes a new Prize Fund for HIV/AIDS. Is the \$3 billion per year fund enough? It would be good to know what the industry is actually spending on R&D for new AIDS drugs.”).

<sup>53</sup> James Love, *How transparency of the costs of clinical trials will improve policy making*, Knowledge Economy International (May 22, 2019), <https://www.keionline.org/30814>.



In short, access to complete, reliable, timely data on the costs of clinical trials will be of value to all those who run clinical trials and to those who fund them. Better understanding the true costs of trials and identification of the primary drivers of the increase in the costs of clinical trials over time, will help make all clinical trials more efficient.

## B. Disaggregated Cost Data Will Enable Better Policymaking

Most existing studies of clinical trial costs report only a periodic, lump-sum, average cost of bringing a drug to market.<sup>54</sup> In a memo opposing transparency into clinical trial costs, the industry trade group BIO<sup>55</sup> contended that “aggregated, de-identified information is often collected by accredited academics to provide periodic estimates of the cost of modern drug development.”<sup>56</sup> In other words, in BIO’s view, there is no reason to require disaggregated cost reporting; occasional estimates of lump-sum expenditures are enough.

However, there are many benefits to greater transparency and sharing disaggregated clinical trial cost data, not just periodic lump-sum estimates. First, there are significant disagreements in the literature as to how final cost should be calculated, as discussed in detail in Section IV. If disaggregated cost data is disclosed instead of simply a final cost estimate, policymakers and the public can evaluate which data points should be included in the final calculation of total cost, and how they should be weighed to reach a final number.

Second, for policymakers to be able to use clinical trial cost data, they must be able to assess the reliability of that data. To do that, experts must have access to the disaggregated data on which the lump-sum estimates are based. We currently lack thorough access to that data, but the limited data we do have suggests that the periodic lump-sum estimates are unreliable because they are funded by the pharmaceutical industry, which has a strong interest in exaggerating clinical trial costs. The civil society organization Knowledge Ecology International (KEI) notes, “At present the large drug companies primarily use the work of the Tufts Center for Drug Development as an

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<sup>54</sup> See, e.g., Donald W. Light, Jon Kim Andrus, and Rebecca N. Warburton, *Estimated research and development costs of rotavirus vaccines*, 27 VACCINE 6627, 6630-31(2009); Joseph A. DiMasi, Henry G. Grabowski, and Ronald W. Hansen, *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. OF HEALTH ECON. 20, 24 (2016).

<sup>55</sup> BIO, or Biotechnology Innovation Organization, is a trade association representing biotechnology companies, academic institutions, state biotechnology centers and related organizations. *BIO’s Vision & Mission*, BIO (last accessed June 23, 2020), <https://www.bio.org/vision-mission>.

<sup>56</sup> Love, *supra* note 48.



industry[-]funded source of data that is spun to benefit industry lobbying efforts, supplemented by a group of economists that PhRMA has referred to as their ‘intellectual echo chamber of economists.’ By ‘accredited academics,’ one has to ask, who provides the accreditation to have access to non-disclosed project level data? The answer, of course, is the PhRMA<sup>57</sup> and BIO member companies who lobby the Congress.”<sup>58</sup>

Third, there are situations in which more specific data is necessary, for which existing periodic lump-sum estimates and high-level aggregated data will not be useful. For example, costs vary significantly among clinical trial phases and therapeutic areas,<sup>59</sup> and costs may be driven by the number of patients and clinic visits required for the trial.<sup>60</sup> One study found that the total cost of running clinical trials for an infectious disease drug candidate was approximately half that of a respiratory system drug candidate.<sup>61</sup> Within the category of respiratory system drug clinical trials—especially relevant given the COVID-19 pandemic—the same study found a Phase 3 trial costs approximately 4.5 times as much as a Phase 1 trial. If grants or prize funds are being offered to successfully develop a particular treatment, it is necessary to have an accurate estimate of how much that drug development might cost.

Lastly, periodic lump-sum estimates are only released every few years, and there are circumstances in which this data will need to be accessed immediately. For example, during the outbreak of a global pandemic such as COVID-19, it would be useful to policymakers to have immediate access to a recent estimate of the costs to develop a vaccine. With this knowledge, they will be better positioned to design policies and appropriate funds to ensure the fastest development of a new vaccine.<sup>62</sup>

### C. Reasons to Focus Specifically on Clinical Trial Cost Transparency at the NIH

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<sup>57</sup> The Pharmaceutical Research and Manufacturers of America, PhRMA, represents the country’s leading biopharmaceutical researchers and biotechnology companies. See generally, PhRMA (last accessed June 23, 2020), <https://www.phrma.org/en>.

<sup>58</sup> Love, *supra* note 48.

<sup>59</sup> Aylin Sertkaya et al., *Examination of Clinical Trial Costs and Barriers for Drug Development*, 3-2 (Jul. 25, 2014), [https://aspe.hhs.gov/system/files/pdf/77166/rpt\\_erg.pdf](https://aspe.hhs.gov/system/files/pdf/77166/rpt_erg.pdf).

<sup>60</sup> Thomas J. Moore et al., *Variation in the estimated costs of pivotal clinical benefit trials supporting the US approval of new therapeutic agents, 2015–2017: a cross-sectional study*, 10 *BMJ OPEN* E038863 (2020), <https://bmjopen.bmj.com/content/10/6/e038863>.

<sup>61</sup> Sertkaya et al., *supra* note 59, at 3-3. See also Moore et al., *id.* (estimating significant variation in the cost of running clinical trials in different disease areas).

<sup>62</sup> Christopher J. Morten, Amy Kapczynski, Harlan M. Krumholz, Joseph S. Ross, *To Help Develop The Safest, Most Effective Coronavirus Tests, Treatments, And Vaccines, Ensure Public Access To Clinical Research Data*, *Health Affairs* (Mar. 26, 2020), <https://www.healthaffairs.org/doi/10.1377/hblog20200326.869114/full/>.



The National Institutes of Health (NIH), part of the U.S. Department of Health and Human Services (HHS), is the U.S.'s primary medical research agency.<sup>63</sup> The NIH is the largest public funder of biomedical research in the world;<sup>64</sup> its budget for fiscal year 2020 is \$41.68 billion.<sup>65</sup> In addition to funding research through grant awards, the NIH runs its own research hospital, called the Clinical Center, in Bethesda, Maryland.<sup>66</sup>

The NIH is composed of many institutes and centers devoted to the study of particular disease areas. For example, two well-known institutes within NIH are the National Cancer Institute (NCI) and National Institute of Allergy and Infectious Diseases (NIAID). Each institute and center receives its own funding appropriation from Congress, and these individual appropriations are included in the overall estimate of the NIH's total budget.<sup>67</sup> Congress does not, however, appropriate funding directly to the Clinical Center, where the NIH's intramural research program is conducted.<sup>68</sup>

This paper focuses on clinical trial cost transparency at the NIH for a number of reasons. First, clinical trials represent the largest percentage of overall R&D expenditures,<sup>69</sup> and as mentioned above, the NIH is the largest public funder of biomedical research in the world. Having reliable data on clinical trial costs will thus provide critical insight into overall R&D costs. This is especially true because NIH spending has contributed to every new drug approved for marketing between 2010 and 2016.<sup>70</sup> The economist Mariana Mazzucato has written (with respect to NIH's entire research activity, not merely clinical trials) that the NIH lies "[a]t the forefront" of

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<sup>63</sup> *Who We Are*, National Institutes of Health (last accessed June 23, 2020), <https://www.nih.gov/about-nih/who-we-are>.

<sup>64</sup> *Impact of NIH Research*, National Institutes of Health (last accessed June 23, 2020), <https://www.nih.gov/about-nih/what-we-do/impact-nih-research>.

<sup>65</sup> *Budget Appropriation for Fiscal Year 2020*, National Institute of Allergy and Infectious Diseases (Jan. 8, 2020). [https://www.niaid.nih.gov/grants-contracts/budget-appropriation-fiscal-year-2020#:~:text=Good%20news%2C%20we%20now%20have.%242.6%20billion%20from%20FY%202019;see also Further Consolidated Appropriations Act, H.R. 1865, 116<sup>th</sup> Cong. \(2020\); Summary of H.R. 1865, United States Senate Committee on Appropriations, 4 \(last accessed June 28, 2020\), \(https://www.appropriations.senate.gov/imo/media/doc/121619%20--%20HR1865%20Domestic%20Intl%20Asst%20Package%20Summary.pdf](https://www.niaid.nih.gov/grants-contracts/budget-appropriation-fiscal-year-2020#:~:text=Good%20news%2C%20we%20now%20have.%242.6%20billion%20from%20FY%202019;see%20also%20Further%20Consolidated%20Appropriations%20Act,%20H.R.%201865,%20116th%20Cong.%20(2020);%20Summary%20of%20H.R.%201865,%20United%20States%20Senate%20Committee%20on%20Appropriations,%204%20(last%20accessed%20June%2028,%202020),%20(https://www.appropriations.senate.gov/imo/media/doc/121619%20--%20HR1865%20Domestic%20Intl%20Asst%20Package%20Summary.pdf).

<sup>66</sup> *About the Clinical Center*, NIH Clinical Center (last accessed June 23, 2020), <https://clinicalcenter.nih.gov/about1.html>.

<sup>67</sup> Further Consolidated Appropriations Act, H.R. 1865, 116<sup>th</sup> Cong. (2020). This year, NCI received \$6.2 billion and NIAID \$5.9 billion, for example. *Id.*

<sup>68</sup> *See id.*

<sup>69</sup> *See, e.g., DiMasi et al., Innovation in the pharmaceutical industry: New estimates of R&D Costs*, 47 J. OF HEALTH ECON. 20, 26 Fig. 3 (Feb. 12, 2016) (finding overall R&D costs nearing \$2.6 billion with clinical costs the largest portion of expenditure at \$1.46 billion).

<sup>70</sup> Ekaterina Galkina Cleary, Jennifer M. Beierlein, Navleen Surjit Khanuja, Laura M. McNamee, and Fred D. Ledley, *Contribution of NIH funding to new drug approvals 2010–2016*, Proceedings of the National Academy of Sciences of the USA (Mar. 6, 2018), <https://www.pnas.org/content/115/10/2329.long>.



government programs that “have invested in many of the key scientific achievements that the [biotech] industry’s success has been built on.”<sup>71</sup>

Second, as such a significant spender of taxpayer dollars on universally important public programs, the NIH should be subject to more budgetary oversight by Congress and the public. The public currently has little insight as to how the NIH manages its own spending or whether it tracks its own intramural research costs in any consistent way. Requiring the NIH to be transparent about its clinical research costs will force it to monitor these costs more closely, which will hopefully result in more cost-effective operation.

Indeed, even as the NIH has been rightfully celebrated for its scientific acumen and leadership, it has at times been criticized for its opacity and imperfect public accountability, ranging from its failures to disclose the results of its own clinical trials<sup>72</sup> to potential conflicts of interest in its extramural grant-making.<sup>73</sup> Expanding its sharing of clinical trial cost data will support public oversight, build trust, and help protect NIH’s credibility.

Additionally, clinical trial cost transparency at the NIH will allow for greater scrutiny of both the NIH’s technology transfer agreements and the clinical trials themselves. While a large funder of biomedical research, NIH does not usually develop drugs or other biomedical products. Instead, it transfers its research to other actors, generally industry firms, who use the knowledge created by government-funded scientists to develop and bring a product to market. These technology transfer agreements have long been favorable to industry partners, and transparency will likely reveal that NIH has not been utilizing its bargaining power to earn a return on its (and therefore the public’s) investments in biomedical research.<sup>74</sup> Tapping the benefits of this transparency will require that the terms of technology transfer agreements also be publicized. That way, the public can monitor its own financial contribution to scientific

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<sup>71</sup> Mariana Mazzucato, *The Entrepreneurial State*, 75 (London: Penguin, 2018).

<sup>72</sup> Charles Piller, *supra* note 31.

<sup>73</sup> Paul D. Thacker, *How a flood of corporate funding can distort NIH research*, Washington Post (Jun. 22, 2019), [https://www.washingtonpost.com/outlook/how-corporate-funding-distorts-nih-research/2018/06/22/ad0260c8-7595-11e8-9780-b1dd6a09b549\\_story.html](https://www.washingtonpost.com/outlook/how-corporate-funding-distorts-nih-research/2018/06/22/ad0260c8-7595-11e8-9780-b1dd6a09b549_story.html); Jocelyn Kaiser, *Three percent of NIH grants involved a direct financial conflict of interest, watchdog report finds*, SCIENCE (Sep. 30, 2019, 5:20 P.M.), <https://www.sciencemag.org/news/2019/09/three-percent-nih-grants-involved-direct-financial-conflict-interest-watchdog-report>.

<sup>74</sup> See, e.g., Zachary Brennan, *NIH’s Exclusive Licenses to Biotech, Pharma Start-Ups: Lots of Secrecy, Few Successes*, Regulatory Focus (May 10, 2016), <https://www.raps.org/regulatory-focus™/news-articles/2016/5/nih’s-exclusive-licenses-to-biotech,-pharma-start-ups-lots-of-secrecy,-few-successes>; Letter from James Love, Kathryn Ardizzone and Luis Gil Abinader of Knowledge Ecology International (KEI) to U.S. Reps. Elijah Cummings and Jim Jordan (Jul. 22, 2019), [https://www.keionline.org/wp-content/uploads/KEI\\_Letter\\_HouseOversightCommittee\\_-NIH\\_Lack\\_of\\_Transparency\\_22July2019.pdf](https://www.keionline.org/wp-content/uploads/KEI_Letter_HouseOversightCommittee_-NIH_Lack_of_Transparency_22July2019.pdf).



developments that ultimately are commercialized by industry and whether it, through the NIH's transfer agreements, receives a fair return on its investment.

Lastly, while R&D cost transparency across all clinical trial funders is the long-term ideal, the NIH is a natural, and critical, starting point. NIH's actions may catalyze more broadly reaching transparency, or may in themselves provide enough data to show that present estimates do not accurately reflect the costs of conducting clinical trials for different therapeutic products across different therapeutic areas. NIH conducts and funds many clinical trials across all disease areas. It would be useful to compare NIH's costs of conducting those trials to the estimates put out by industry-funded studies, such as the well-known DiMasi studies, which estimate the cost of developing a single drug at \$2.6 billion.<sup>75</sup> Since the inputs to industry estimates of R&D costs are not disclosed, policymakers and the general public have no way of knowing what they include or if they are accurate. Understanding the breakdown of NIH's clinical trial costs will illuminate where industry either overspends or is overinclusive in its own cost calculations.<sup>76</sup> Expanding sharing of clinical trial cost data may also permit independent analysts to develop reliable estimates of the respective costs of conducting clinical trials in industry, academia, and NIH's own facilities, something that has proven difficult with the limited data currently available publicly.<sup>77</sup> Such a comparison may show that

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<sup>75</sup> See Joseph A. DiMasi et al., *Cost of Innovation in the Pharmaceutical Industry*, 10 J. OF HEALTH ECON. 107 (1991); DiMasi et al., *supra* note 69. A more recent estimate has even reached \$3.2 billion. Robert D. Atkinson, *How the Biopharmaceutical Industry Contributes to Open Scientific Knowledge*, Information Technology & Innovation Foundation (Nov. 2018), [http://www2.itif.org/2018-biopharmaceutical-open-knowledge.pdf?\\_ga=2.100530070.961923108.1592327010-645292166.1591967991](http://www2.itif.org/2018-biopharmaceutical-open-knowledge.pdf?_ga=2.100530070.961923108.1592327010-645292166.1591967991).

<sup>76</sup> To be sure, the costs of conducting clinical trials at NIH and its grantee institutions (e.g., an academic medical center) may not always be directly comparable to the costs of industry-sponsored trials. For example, the rigorously documented “pivotal” clinical trials designed to support regulatory approvals (e.g., approval by the U.S. Food and Drug Administration (FDA) and European Medicines Agency) may be somewhat more complex and expensive to conduct than trials undertaken purely for research purposes. See Linda Martin *et al.*, *How Much Do Clinical Trials Cost?*, 16 NATURE REVIEWS DRUG DISCOVERY 381 (2017). While some pivotal trials have been funded by the NIH—see, e.g., *Daily HIV prevention approaches didn't work for African women in the VOICE study*, Medical Xpress (Mar. 4, 2013), <https://medicalxpress.com/news/2013-03-tenofovir-vaginal-gel-daily-dosing.html>—most are not. Industry sponsors may sometimes have different incentives than NIH and other non-profit clinical trial sponsors—e.g., to avoid liability under tort law, or to arrange the involvement of key medical “opinion leaders”—and may therefore design and conduct trials differently. See, e.g., Anna C. Mastroianni, *HIV, Women, and Access to Clinical Trials: Tort Liability and Lessons from DES*, 5 DUKE J. OF GENDER L. & POLICY 167 (1998) (describing historical exclusion of women from clinical trials in industry-sponsored clinical trials to reduce perceived risk of tort liability); Ray Moynihan, *Key opinion leaders: independent experts or drug representatives in disguise?*, 336 (7658) BMJ 1402 (2008) (suggesting that drug companies may pay “opinion leaders” high fees for participation in clinical trials as a way to market their drugs). Nonetheless, we believe that NIH's clinical trial cost data is a useful starting point for comparison.

<sup>77</sup> See, e.g., Marcela Vieira, *Research Synthesis: Costs of Pharmaceutical R&D*, v.1.0, Knowledge Portalia (Jan. 2020), <https://www.knowledgeportalia.org/cost-of-r-d> (noting that a current “Research gap” is inclusion of “[m]ore studies on R&D costs from not-for-profit product development organizations (e.g. public institutions, academia and product development partnerships”).



conducting clinical trials at NIH rather than in industry is ultimately more cost-effective from the public's perspective.<sup>78</sup>

The cost data that the NIH already discloses, such as grant awards,<sup>79</sup> overall yearly clinical expenditures,<sup>80</sup> and other reports,<sup>81</sup> is not sufficient to inform the public of its clinical trial expenditures, as we show below. In fact, current cost reporting by the NIH is frequently insufficient to understand even the aggregate costs of some clinical trials.

#### IV. THE IDEAL: WHAT DATA IS NEEDED?

This section proposes specific data points that should be reported by the NIH to allow for accurate evaluation and comparison of clinical trial costs. To frame this discussion, we will first examine previous estimates of R&D costs, focusing on the data sources they used and how they evaluated and weighed the data to arrive at an overall estimate of the cost to run a clinical trial or develop a drug. We then discuss potential data points and narrow our proposed list to precise, discrete data points on the costs of clinical trials that are most useful to calculate accurate clinical trial cost estimates. Finally, we discuss other factors that have been included or excluded by various authors and organizations, such as capital costs, costs of failures, external funding, and tax benefits. While we do not propose to settle the debate about how to reach a final cost estimate, we suggest that increasing the number of publicly available data points will allow for economists and health policy experts to better assess the merits of the methodologies and their critiques and ultimately arrive at more accurate estimates of clinical trial costs.

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<sup>78</sup> See, e.g., Michael S. Sinha, Mehdi Najafzadeh, Elizabeth K. Rajasingh, et al., *Labeling Changes and Costs for Clinical Trials Performed Under the US Food and Drug Administration Pediatric Exclusivity Extension, 2007 to 2012*, 178 JAMA INTERNAL MED. 1458 (Nov. 2018), <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2702288> (suggesting “direct funding of pediatric trials through the National Institutes of Health (NIH)” rather than relying on industry to conduct these trials).

<sup>79</sup> Funding data for individual grants is available through RePORTER. Query Form, NIH RePORT (last accessed June 23, 2020), <https://projectreporter.nih.gov/reporter.cfm>.

<sup>80</sup> *NIH Clinical Center Data Report 2019: Report on 2018 Activities* (2019), [https://clinicalcenter.nih.gov/about/\\_pdf/2019CCDataReport.pdf](https://clinicalcenter.nih.gov/about/_pdf/2019CCDataReport.pdf).

<sup>81</sup> *Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC)*, (Feb. 24, 2020), [https://report.nih.gov/categorical\\_spending.aspx](https://report.nih.gov/categorical_spending.aspx); *Biennial Report of the Director, National Institutes of Health Fiscal Years 2014 & 2015* (last updated June 13, 2018), <https://report.nih.gov/biennialreport/>; *NIH Data Book* (last accessed June 23, 2020), <https://report.nih.gov/nihdatabook/index.aspx>.



## A. Sources of Data in Previous Studies of R&D Costs

There have been many estimates of R&D costs since at least the 1970s.<sup>82</sup> While it is beyond the scope of this report to do a comprehensive literature review of previous R&D estimates,<sup>83</sup> we will highlight the data sources and costs included by previous researchers to illustrate why it is important to have a reliable source of disaggregated cost data from clinical trials. Notably, while the NIH is the largest funder of clinical trials in the world,<sup>84</sup> its data is largely missing from the leading estimates of the costs of running clinical trials.

### 1. Use of Industry-Reported Data

Several studies use self-reported data from pharmaceutical companies. For example, all seven studies performed by DiMasi and colleagues between 1991 and 2016 used data obtained via confidential surveys of industry firms<sup>85</sup> and a proprietary database belonging to the Tufts University Center for the Study of Drug Development.<sup>86</sup>

In these studies, the use of industry-reported data obscures the question of which data points are actually included in the calculation of overall costs, how that data is collected and validated, and how the calculation is performed.<sup>87</sup> And while our proposal to disclose disaggregated cost data for NIH-funded clinical trials will not necessarily change or clarify the data points used in future estimates based on industry-reported data, NIH data might provide useful comparators across the wide range of

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<sup>82</sup> See, e.g., Joseph A. DiMasi et al., *Cost of Innovation in the Pharmaceutical Industry*, 10 J. OF HEALTH ECON. 107, 111 (1991) (describing early estimates of pharmaceutical R&D costs).

<sup>83</sup> Many sources have done so. See, for example, Marcela Vieira, *Research Synthesis: Costs of Pharmaceutical R&D* (2020) for a recent and comprehensive analysis. For an analysis of estimates through DiMasi et al.'s 2016 report, see MSF, *Lives on the Edge*, *supra* note 2 at Annex 1.

<sup>84</sup> See William Jackson, *NIH Builds a Bridge to Paperless Processes*, FCW (Sep. 30, 2010), <https://fcw.com/Articles/2010/10/04/NCI-Bridges.aspx?Page=2> (noting that the National Cancer Institute, an institute within the NIH, is “the world’s largest sponsor of clinical trials”).

<sup>85</sup> The survey instrument used in the 2016 study included four components to be filled out by the surveyed firms: Annual Pharmaceutical R&D Expenditures, 1990-2010; R&D Expenditures by Stage of Development; a questionnaire regarding whether overhead is included and if so, what the amount is, how capital expenditures are reported, and whether charges or rents for facilities are included; and R&D Time and Expenditure Portfolio: Testing Time Profile and Testing Expenditure Profile by Year and Stage of Development. DiMasi et al., *supra* note 69 at Appendix G.

<sup>86</sup> *Id.*

<sup>87</sup> See Donald W. Light & Rebecca Warburton, *Demythologizing the High Costs of Pharmaceutical Research*, 6 *BioSocieties* 34, 38 (2011) (noting that, for the DiMasi studies, “[o]ne does not know how companies calculated their R&D costs or what they included”); see also *id.* (describing potentially divergent methods of identifying and counting R&D costs and listing costs that might be included by some firms and not others).



therapeutic areas in which NIH conducts and funds research and set the standard for future industry-reported data disclosures.

## 2. Use of Unique Data from Non-Profit Drug Development Initiatives

The Drugs for Neglected Diseases *initiative* (DNDi), a non-profit pharmaceutical research and development organization that focuses on new treatments for neglected diseases, estimates R&D costs based on its own self-reported data in the report *15 Years of Needs-Driven Innovation for Access*.<sup>88</sup> DNDi prioritizes transparency and has disclosed not just its costs but the methodology it uses to calculate those costs, including the costs of its clinical trials.<sup>89</sup> However, DNDi acknowledges that its business model is unique for many reasons—for example, DNDi sometimes receives in-kind contributions from industry partners, such as donated drugs, that reduce DNDi's trial costs—and that it is accordingly difficult to compare DNDi's clinical trial costs to those incurred by industry, government, and academic laboratories.<sup>90</sup>

## 3. Use of Proprietary Databases

Some studies rely on clinical trial cost data contained in proprietary, for-profit databases. Among other sources, Sertkaya *et al.* used Medidata Solutions databases to “obtain[] itemized clinical trial cost data . . . which compiles data from a portfolio of CRO [contract research organization] contracts, investigator grants/contracts, and clinical trial protocols.”<sup>91</sup> Contract research organizations are firms that partner with pharmaceutical companies to conduct clinical trials.<sup>92</sup> While this data is perhaps more likely to be reliable than self-reported data, since it is aggregated and presumably verified by an objective third party, a big drawback is that this information is not publicly accessible.

## 4. Use of Publicly Available Data

Other studies use data from a variety of publicly-available sources, including the U.S. Food and Drug Administration (FDA)'s Drugs@FDA database, the NIH's

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<sup>88</sup> See Drugs for Neglected Diseases *initiative*, *15 Years of Needs-Driven Innovation for Access*, 17-20 (2019). The DNDi report, notes that their estimates “excluding discovery and including registration” are “[f]ully loaded” and “includ[e] management and indirect costs.” *Id.* at 20.

<sup>89</sup> See Drugs for Neglected Diseases *initiative*, *An Innovative Approach to R&D for neglected patients: ten years of experience & lessons learned by DNDi*, 18 (2013).

<sup>90</sup> *Id.* at 20 (stating that “it is difficult to compare costs of development between different business models”).

<sup>91</sup> Sertkaya *et al.*, *supra* note 59 at 2-9.

<sup>92</sup> See Our Mission, Association of Clinical Research Organizations, (last accessed June 23, 2020), <https://www.acrohealth.org/our-mission/>.



ClinicalTrials.gov, the U.S. Patent and Trademark Office (USPTO)'s Patent and Full-Text Database (PatFT), filings with the U.S. Securities and Exchange Commission (SEC), publications available through Medline, and other internet-based resources. Light *et al.*, for instance, used PatFT, SEC filings, Medline, periodicals, and corporate websites to make estimates on the R&D costs of rotavirus vaccines.<sup>93</sup> Wouters *et al.* analyzed data from the SEC, Drugs@FDA database, ClinicalTrials.gov, and published data on clinical trials success rates.<sup>94</sup>

Of the government-administered public sources in this section, only SEC filings provide actual cost data. The information on forms filed with the SEC has two major limitations: first, only publicly-traded U.S. companies are required to report, and, second, large companies commonly disclose only R&D expenditures across all drug candidates, or across a therapeutic area, rather than costs of testing individual drugs in individual trials.<sup>95</sup> For instance, in their recent estimate, which was based on SEC filing data, Wouters *et al.* excluded products developed by private U.S. pharmaceutical companies and “products developed by companies that only reported total research and development expenditures across all drug candidates or across therapeutic areas.”<sup>96</sup> As a result, only 63 drugs and biologics from 47 companies were included out of 355 FDA approvals for the study's time period.<sup>97</sup>

While the proposals advanced in this section to make costs for NIH-funded clinical trials transparent will not address all concerns with the aforementioned methodologies, it will have substantial benefits for economists and policymakers by adding a large set of reliable data with which to work.

## B. Necessary Data to Evaluate Clinical Trial Costs

First, a preliminary note about grant funding at the NIH is useful. There are two categories of clinical trials that NIH funds that are relevant to this paper: (1) intramural studies, or studies run and conducted entirely by the NIH, and (2) extramural studies, or studies conducted or run, in whole or in part, by other entities that receive some amount of NIH funding. More than 80 percent of NIH's funding is awarded for extramural research, and approximately 10 percent of the NIH's budget supports intramural

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<sup>93</sup> Donald W. Light, Jon Kim Andrus & Rebecca N. Warburton, *Estimated Research and Development Costs of Rotavirus Vaccines*, 27 VACCINE 6627, 6629 (2009).

<sup>94</sup> Oliver J. Wouters, Martin McKee, & Jeroen Luyten, *Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018*, 323 J. AM. MED. ASSOC. 844, 844 (2020).

<sup>95</sup> *Id.* at 845.

<sup>96</sup> *Id.* It appears that any excluded products that had licensing deals with firms who did report R&D data were then included based on the licensee's data. *Id.*

<sup>97</sup> *Id.* at 844.



research. We propose disclosure of cost data for *all* trials that receive any NIH funding, which includes both intramural and extramural research. But it is important to note that the NIH grant forms discussed throughout this section only apply to extramural research activities.

## 1. Proposed List of Disaggregated Data Points

In order to achieve an accurate understanding of clinical trial costs, there must be a breakdown of the discrete data points incorporated in the final estimate. Though the ideal data points may vary by disease area and study phase, we propose a general list that is applicable to most Phase 2-4 clinical trials. In this section, we will walk through the process we used to narrow down a set of recommended data points, acknowledging that our final recommendation may be further refined by other researchers.

All of our recommended legal and policy reforms, discussed in Section VI, can be implemented with any final list of data points; the precise list of data points selected for disclosure does not control our recommendations.

### i. Most Detailed Disaggregated Data Points

We began our investigation into how cost disclosures should be disaggregated with the following data points, which were compiled based on expert interviews and NIH grant reporting forms<sup>98</sup>:

- Data collection, management, and analysis costs (per study)
- Cost per Institutional Review Board (IRB) approval
- Number of IRB approvals (per study)
- Cost per IRB amendment
- Number of IRB amendments (per study)
- Source data verification (SDV) cost (per data field)
- Number of SDV fields (per study)
- Patient recruitment costs (per patient)
- Patient retention (per patient)
- RN/CRA costs (per patient)
- Physician costs (per patient)
- Clinical procedure total (per patient)
- Central lab costs (per patient)

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<sup>98</sup> See Sertkaya, et al., *supra* note 59; *General Application Guide for NIH and Other PHS Agencies, G.300 - R&R Budget Form*, NIH Grants and Funding (Dec. 7, 2018), <https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/general/g.300-r&r-budget-form.htm#F>.



- Number of patients (per site)
- Site recruitment costs (per site)
- Site retention costs (per month)
- Number of site management months
- Administrative staff costs (per month)
- Number of project management months
- Site monitoring costs (per day)
- Number of site monitoring days
- Site overhead (per month)
- Number of sites (per study)
- Equipment
- Travel
- Participant/trainee support costs
- Other direct costs
  - Materials and supplies
  - Publication Costs
  - Consultant Services
  - ADP/Computer Services
  - Subawards/Consortium/Contractual Costs
  - Equipment or Facility Rental/User Fees
  - Alterations and Renovations
  - Other
- Indirect costs

## ii. Narrowing Down of Data Points

This breakdown of data would allow the most careful scrutiny of reported costs. However, after extensive research and interviews with researchers, economists, access-to-medicines advocates, and other experts, we determined that it may be too burdensome for the NIH to collect and verify cost data or for a clinical trial sponsor to calculate and disclose cost data at this level of granularity. Therefore, we looked at three factors to reach a final, shorter list of proposed data points: (1) the top drivers of clinical trial costs, (2) specific data points that are already collected by NIH and other clinical trial sponsors (making them easier to disclose), and (3) cost categories that reveal key information, even if not themselves top drivers of total costs.

In order to understand and scrutinize the true costs of conducting a clinical trial, it is important to know which components are most costly and accurately disaggregate those components. According to a 2014 study submitted to the United States Department of Health and Human Services (HHS), “the top cost drivers of clinical trial



expenditures across all study phases are Clinical Procedure (15 to 22 percent), Administrative Staff (11 to 29 percent), Site Monitoring (nine to 14 percent), Site Retention (nine to 16 percent), and Central Laboratory (four to 12 percent) costs.”<sup>99</sup>

We also considered how the NIH collects cost information from its grantees, reasoning that if certain disaggregated data is already tracked by NIH grantees and the NIH itself, the data would be less burdensome to collect, maintain, and disclose. “The R&R Budget Form,” used for grant applications, contains a detailed list of budgetary estimates, including:<sup>100</sup>

- Personnel costs (including salary and benefits)
- Equipment
- Travel
- Participant/trainee support costs
- Other direct costs
  - Materials and supplies
  - Publication Costs
  - Consultant Services
  - ADP/Computer Services
  - Subawards/Consortium/Contractual Costs
  - Equipment or Facility Rental/User Fees
  - Alterations and Renovations
  - Other
- Indirect costs

Lastly, we learned in conversations with experts<sup>101</sup> that there are other data points that are crucial to understanding the true costs of conducting clinical trials. Firstly, all data must be reported on a yearly basis because costs can vary significantly by year.<sup>102</sup> Secondly, it is important to disclose costs per patient, as this may vary

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<sup>99</sup> Sertkaya, *et al.*, *supra* note 59 at 3-5 – 3-7. We note that these estimates of cost drivers exclude both site overhead and a catch-all category of all other costs not captured in the specific data points obtained for the study.

<sup>100</sup> *General Application Guide for NIH and Other PHS Agencies, G.300 - R&R Budget Form*, *supra* note 98.

<sup>101</sup> The experts with whom we consulted included Jamie Love, Claire Cassidy, Kathryn Ardizzone & Luis Gil Abinader of Knowledge Ecology International; Dana Gill & Gaëlle Krikorian of MSF; Adrian Towse of the Office of Health Economics in the United Kingdom; Anna Birkenbach of the University of Delaware; Jack Scannell of JW Scannell Analytics; Suerie Moon, Marcela Vieira & Temmy Sunyoto of the Graduate Institute (Geneva, Switzerland); and Laurence Vielfaure & Rachel Cohen of the Drugs for Neglected Diseases *initiative*.

<sup>102</sup> This becomes important for accurate calculations of the cost of capital, should the researcher choose to use this measure of total cost. See *KEI Memo on U.S. Legislation to cap price increases on prescription drugs and to enhance the transparency of R&D costs*, Knowledge Ecology International (Apr.



significantly among trial phases and therapeutic areas. We do not foresee that tracking costs by year or costs per patient will increase the administrative burden on clinical trial sponsors or the NIH, as it is standard to track financial information by the year and standard to track the number of patients enrolled throughout a trial.

### iii. Final Recommended List of Disaggregated Data Points

After considering the various data points and factors discussed above, we recommend that the following specific data points be disclosed for all clinical trials funded in whole or in part by the NIH. (We reiterate, however, that all of our recommended legal and policy reforms, discussed below in Section VI, can be implemented with any final list of data points; the precise list of data points selected for disclosure does not control our recommendations. Legislators and policymakers, working in concert with experts, may decide that a different list of disaggregated data points is best to disclose.)

Costs to be reported for the overall study, per patient, per year, and (if possible) per site:

- Personnel costs (including salary and benefits)<sup>103</sup>
  - Administrative staff
  - Clinical staff
- Materials and supplies
- Clinical procedures<sup>104</sup>
- Site management
  - Site monitoring costs
  - Site retention
  - Other
- Central laboratory
- Equipment
- Other direct costs
  - Publication costs
  - Subawards/consortium/contractual costs
  - Other
- Indirect costs

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13, 2019), <https://www.keionline.org/30578> (“Estimates of capital costs depend upon when trial costs are incurred.”). See Section IV.2, *infra*, for a further discussion of the cost of capital.

<sup>103</sup> We note that the R&R Budget Form requires individual salary reporting, and we do not suggest the NIH publish this sensitive information. Instead, the NIH should publish a sum of all salary and benefit information for the trial.

<sup>104</sup> We use the term “clinical procedures” broadly, to cover any and all practices of health care practitioners to care for individual patients.



## 2. Other Relevant Factors

In addition to specific, disaggregated dollar amounts spent on a clinical trial, there are other factors that contribute to the final cost of that trial. Though the following data points do not all necessarily apply to a government agency such as the NIH, we discuss the broadest range of cost data that can be collected and reported on clinical trials.

There is some disagreement in the literature over which data points are relevant, and not all studies rely on the same set of data points. Some studies, mostly industry-funded and particularly the DiMasi studies, have incorporated additional data points preferred by industry. Two especially controversial inclusions in DiMasi's overall cost estimates are the opportunity cost of capital and costs of failures.<sup>105</sup> While we do not take a position on how best to perform the ultimate calculation of the cost of a particular clinical trial, we discuss what information should be disclosed in order to provide a complete set of inputs for that ultimate calculation.

In their 1991 study, DiMasi *et al.* explain that an expected capitalized cost must be added to out-of-pocket costs for a given trial “[t]o include the opportunity cost of funds invested in NCE [new chemical entity] R&D for a full cost estimate.”<sup>106</sup> The actual out-of-pocket costs of a clinical trial is multiplied by a certain factor<sup>107</sup>—9% per year in the 1991 DiMasi study—compounded for the estimated time from the beginning of Phase 1 of a new drug study to the date of marketing approval in order to account for the missed opportunity of simply investing that dollar amount.<sup>108</sup> DiMasi *et al.* explain the inclusion of this multiplier by classifying R&D as an investment cost. Subsequent studies have criticized the treatment of R&D as an investment cost as not in accordance with the “generally accepted accounting principles” that govern income tax filings, which benefit the taxpayer by classifying research costs as a deduction to be taken in the year incurred, not an investment to be capitalized over time.<sup>109</sup> In order to ensure a clearer

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<sup>105</sup> See, e.g., MSF, *Lives on the Edge*, *supra* note 2 at Annex 1; Light & Warburton, *supra* note 87, at 41.

<sup>106</sup> Joseph A. DiMasi, et al., *Cost of Innovation in the Pharmaceutical Industry*, 10 J. OF HEALTH ECON. 107 (1990).

<sup>107</sup> The figure used attempts to approximate the company's expected returns had that money been placed into the stock market. See Light & Warburton, *supra* note 87 at 37.

<sup>108</sup> *Id.*

<sup>109</sup> Merrill Gozner, *The \$800 Million Pill: The Truth Behind the Cost of New Drugs* (2004); see also Light *et al.*, *Estimated research and development costs of rotavirus vaccines*, 27 VACCINE 6627, 6628 (Aug. 7, 2009) (“While estimating profits forgone is a useful calculation for making investment decisions, their inclusion in total R&D costs as a claim against public bodies and society is questionable. These companies need to innovate to maintain profits; they are not in the business of simply investing funds. In addition, R&D costs are treated by the IRS as a normal business expense that is deducted from gross



picture of clinical trial costs, therefore, sponsors must report tax savings realized by deducting R&D costs. Furthermore, clinical trial costs can vary significantly by year, which affects this cost of capital calculation. In order to be more precise in calculating the cost of capital, per-year clinical trial costs must be disclosed.

Costs of failures, while also not specifically associated with any given clinical trial, are out-of-pocket costs incurred by the trial sponsor. DiMasi's 1991 study predicts a 23 percent success rate based on proprietary, undisclosed data.<sup>110</sup> This is factored into his overall cost estimate by dividing the prior calculated cost of investigational drugs by 0.23 to reach the total cost for approved drugs.<sup>111</sup> Despite a recognition that failure rates decrease and cost per phase increases as drugs move through each clinical trial phase, DiMasi *et al.* do not appear to account for this in their calculation of the effect of failure rates on overall cost. To accurately account for costs of failures, clinical trial sponsors must disclose the dollar amount spent on failures, disaggregated by the data points proposed in the following sub-section, the regulatory phase at which the drug failed, and whether the drug failed to meet the necessary outcome measures for FDA approval or whether development was discontinued for other reasons.

Studies conducted by researchers and organizations interested in promoting access to medicines have suggested incorporating different data in overall cost estimates.<sup>112</sup> Specifically, access to medicines advocacy groups have proposed including external funding contributions and all relevant tax benefits. For example, KEI advocates disclosure and incorporation of the following funding contributions: the NIH grant or contract; any other federal agency; any other non-federal government agency; any charities, industry, and health plans that provide reimbursement of trial related expenses.<sup>113</sup> Additionally, Public Citizen has pointed out that the widely-cited DiMasi estimates do not account for R&D tax credits enjoyed by the drug industry.<sup>114</sup> According

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income annually, reducing current taxes; but tax savings are not reflected in the \$802 million figure. Thus the methods developed to convert \$87 million to \$802 million are not without controversy and have been the subject of published critiques by ourselves and others. Any estimate of returns on investment before the fact might more usefully be regarded as a goal, rather than a guarantee or claim on society.”)

<sup>110</sup> DiMasi, et al., *Cost of Innovation in the Pharmaceutical Industry*, 10 J. HEALTH ECON. 107 (1991).

<sup>111</sup> *Id.*

<sup>112</sup> E.g., Light & Warburton, *supra* note 87; James Love, *KEI comments on DRAFT NIH Policy for Data Management and Sharing and Supplemental DRAFT Guidance*, Knowledge Economy International (Jan 13, 2020), <https://www.keionline.org/32112>; *Rx R&D Myths: The Case Against The Drug Industry's R&D "Scare Card"*, Public Citizen Congress Watch (2001); Goozner, *supra* note 109, at Ch. 9; MSF, *Lives on the Edge*, *supra* note 2.

<sup>113</sup> James Love, *KEI comments on DRAFT NIH Policy for Data Management and Sharing and Supplemental DRAFT Guidance*, Knowledge Economy International (Jan. 13, 2020), <https://www.keionline.org/32112>.

<sup>114</sup> *Rx R&D Myths: The Case Against The Drug Industry's R&D "Scare Card"*, Public Citizen Congress Watch (2001).



to the Congressional Office of Technology Assessment (OTA), “[t]he net cost of every dollar spent on R&D must be reduced by the amount of tax avoided by that expenditure. Like all business expenses, R&D is deductible from a firm’s taxable income.”<sup>115</sup> In addition to standard deductions for R&D costs incurred in a given year, the pharmaceutical industry enjoys four tax credits: the foreign tax credit, possessions tax credit, research and experimentation tax credit, and the orphan drug tax credit.<sup>116</sup> According to a Congressional Research Service report published in 1999, these tax credits allowed the drug industry to save \$4 billion per year in taxes.<sup>117</sup> A Government Accountability Office report published in 2017 similarly states that the pharmaceutical industry claimed over \$2 billion in tax credits in 2014 based on two tax credits alone—the orphan drug and research and experimentation tax credits.<sup>118</sup>

We discuss this disagreement not to resolve it here but simply to acknowledge the wide range of data points on clinical R&D costs that have been considered in the literature. We believe that the set of data points we have identified above are indisputably important in calculating the true costs of clinical R&D and in projecting future costs.

We further recommend, given the existing lack of consensus on how to calculate total R&D costs, disclosure by clinical trial sponsors of the following cost information: (1) R&D tax credits, (2) disaggregated costs of R&D for failed candidates, and (3) other funding contributions, including insurance reimbursements. Disclosure of this data will allow for transparency into how the final costs of drug development are calculated, in addition to transparency into what those costs are. Though this paper primarily addresses disclosure of cost data by the NIH, and we leave to future work the question of how best to ensure its disclosure, we encourage all relevant parties to report this list of data points; if shared consistently, this information will benefit all stakeholders by creating a universal starting point from which to have a meaningful and productive discussion on a broad range of issues.

## V. EXISTING DISCLOSURE BY THE NIH IS INSUFFICIENT

The NIH currently collects, retains, and publishes certain information related to clinical trials. While some of this reporting is mandated by law, NIH appears to publish

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<sup>115</sup> *Id.* Appendix 1.

<sup>116</sup> *Id.* at 15.

<sup>117</sup> *Id.* citing Congressional Research Service Memorandum, *Federal Taxation of the Drug Industry* (1999).

<sup>118</sup> *Drug Industry: Profits, Research and Development Spending, and Merger and Acquisition Deals*, U.S. Government Accountability Office, 37-39 (Nov. 2017), <https://www.gao.gov/assets/690/688472.pdf>.



some of it voluntarily. Information on NIH-funded research activities appears in the following array of databases and reports, which we describe in detail below:

- ClinicalTrials.gov: a public database administered by the NIH containing clinical trial data. Most clinical trials, whether NIH-funded or not, must be registered on the website and report certain results there.
- RePORTER: a database administered by the NIH containing certain information about NIH grant awards, usually including the dollar amount of the award and a project description.
- The Data Book: a website administered by the NIH that provides summary statistics of NIH research activities in graphical form.
- The intramural database: a database administered by the NIH containing certain information about NIH intramural research. It does not contain cost information.
- Certain reports to Congress required to be submitted by the NIH, including retrospective reviews of research conducted and prospective strategic plans for future research.
- FOIA requests: used to obtain certain detailed information about individual studies or grants.

Although all of these tools are informative, they do not—alone or combined—provide a clear picture of disaggregated clinical trial costs. First of all, none provide disaggregated cost information. Secondly, even if one could use multiple sources to piece together certain data, the process is difficult and would not achieve the broad, sustained cost transparency this paper advocates.

#### A. ClinicalTrials.gov

Under 42 U.S.C. § 282(j), the Director of the NIH must maintain a database of clinical trials. The database must be searchable by various relevant criteria, and “[t]he Director of the NIH shall ensure that the registry data bank is easily used by the public, and that entries are easily compared.”<sup>119</sup> As part of the Food and Drug Administration Amendments Act (FDAAA) in 2007, Congress mandated significantly greater public access to clinical trial information and required large numbers of clinical trials be registered on ClinicalTrials.gov and, for the first time, required clinical trial results be made publicly available there.<sup>120</sup> To fulfill this obligation, the NIH created ClinicalTrials.gov. Most drug and medical device clinical trials must be registered on the

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<sup>119</sup> 42 U.S.C. § 282(j)(2)(B).

<sup>120</sup> Pub. L. No. 110-85, § 801, 121 Stat. 823, 904-22 (codified at 42 U.S.C. § 282(j)). FDAAA significantly expanded the scope of ClinicalTrials.gov, but ClinicalTrials.gov predates FDAAA; ClinicalTrials.gov was first created pursuant to the Food and Drug Administration Modernization Act, enacted in 1997.



website and report certain information at prescribed time periods. The NIH is responsible for administering ClinicalTrials.gov and shares responsibility with the FDA to ensure compliance with reporting requirements.

Congress defined a broad set of “applicable clinical trials” for which the trial sponsors—named “responsible parties”—are required to submit information to be posted on the ClinicalTrials.gov website. The statute defines an applicable clinical trial as any prospective clinical study of health outcomes comparing an intervention with a medical device that is subject to FDA clearance with a control group, or any controlled clinical investigation of drugs that are subject to FDA approval or licensure, with few exceptions.<sup>121</sup> In practice, this means that the vast majority of interventional Phase 2, Phase 3, and Phase 4 trials are applicable clinical trials now required to disclose information on ClinicalTrials.gov.

When a trial is registered, the responsible party must submit certain information to be published on ClinicalTrials.gov, such as the study’s purpose, design, primary disease target, dates and duration, outcome measures, and recruitment information.<sup>122</sup> In addition, upon study completion, responsible parties must at minimum submit “basic results” for applicable clinical trials. Basic results include certain patient characteristics, primary and secondary outcomes, and a point of contact for further information.<sup>123</sup>

Beyond defining basic results and requiring that they be reported for all FDA-approved products, the statute defines a second category of clinical trial results to which the public has a right of access: “expanded results.”<sup>124</sup> There are a few statutory requirements for expanded results, but the statute primarily delegates authority to HHS to define specific reporting requirements and the overall scope of expanded results.<sup>125</sup> The Final Rule promulgated by HHS and NIH is codified at 42 C.F.R. § 11 and imposes certain reporting requirements on responsible parties. Among other things, it defines the scope of expanded results to require that responsible parties report certain information not encompassed by basic results, such as statistical analyses for each outcome measure.<sup>126</sup>

The statute imposes further obligations on NIH when NIH funds a clinical trial “in whole or in part” and specifies requirements and compliance enforcement mechanisms

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<sup>121</sup> *Id.* at § 282(j)(1)(A).

<sup>122</sup> *Id.* at § 282(j)(2)(A).

<sup>123</sup> *Id.* at § 282(j)(2)(C).

<sup>124</sup> *Id.* at § 282(j)(3)(D).

<sup>125</sup> *Id.* at § 282(j)(3)(D)(iii)(I)-(IV).

<sup>126</sup> See 42 C.F.R. § 11.48.



beyond those of non-NIH responsible parties.<sup>127</sup> The heads of such agencies within HHS, including NIH, “shall verify that the clinical trial information for each applicable clinical trial for which a grantee is the responsible party has been submitted . . . before releasing any remaining funding for a grant or funding for a future grant to such grantee.”<sup>128</sup> The Director of the NIH is thus compelled, in addition to publishing all ClinicalTrials.gov submissions, to ensure any applicable clinical trials conducted with NIH funding are reported timely, accurately, and completely, and to withhold future funding if proper reports are not made. This suggests Congressional intent that research funded with taxpayer dollars be documented by NIH and monitored thoroughly by both NIH and the public. In addition, the NIH has mandated in its “Policy on the Dissemination of NIH-Funded Clinical Trial Information” that “all NIH-funded awardees and investigators conducting clinical trials funded in whole or in part by the NIH regardless of study phase, type of intervention, or whether they are subject to the statute and to the rule” must register clinical trials and report results on ClinicalTrials.gov.<sup>129</sup>

While there is currently no cost reporting through ClinicalTrials.gov, it would be an ideal medium through which to report clinical trial costs. ClinicalTrials.gov is relatively simple to navigate and designed to be user-friendly. All registered clinical trials are searchable by condition or disease, recruitment status, site locations, and a unique identifier called the NCT number. Once the user reaches the page for a particular clinical trial, she can navigate to various data entries by category on the “Study Details” page. There is an alternative “Tabular View,” which displays the same information in chart form. Lastly, there is the “Study Results” tab, which displays detailed results of the clinical trial, once they are submitted by the responsible party. Adding a field for cost data on either the “Study Details” or “Study Results” tab would allow any interested person to locate such information readily.

Although neither the statute nor associated rules explicitly require reporting the costs of applicable clinical trials, whether conducted at the NIH or elsewhere, the broad grant of power to the Secretary of HHS and, by proxy, the Director of the NIH to define expanded results suggests that either one has the statutory authority to require cost reporting.<sup>130</sup> The statute already mandates a database structure for required clinical trial submissions and vests enforcement responsibility in the NIH,<sup>131</sup> and there is already

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<sup>127</sup> 42 U.S.C. § 282(j)(5)(A)(i).

<sup>128</sup> *Id.* at § 282(j)(5)(A)(ii).

<sup>129</sup> *NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information*, NIH Grants and Funding (Effective Jan. 18, 2017), <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-149.html>.

<sup>130</sup> *Id.* at § 282(j)(3)(D).

<sup>131</sup> *Id.* at § 282(j)(5).



high compliance with clinical trial registration requirements,<sup>132</sup> although high compliance with results reporting requirements has not yet been achieved, due to a lack of enforcement by the NIH and FDA.<sup>133</sup> Lastly, the requirement for additional monitoring and enforcement mechanisms for any government-funded research conveys Congress's particular emphasis on transparency in clinical trials supported by taxpayer dollars.

## B. RePORT

As a part of the NIH Reform Act of 2006, Congress directed the creation of an “electronic system to uniformly code research grants.”<sup>134</sup> To meet this statutory obligation, the NIH developed a collection of online tools through their “Research Portfolio Online Reporting Tools” (RePORT) website.<sup>135</sup> While the agency stated, in connection with a description of the launch of RePORT, that the “NIH is committed to promoting a high level of public accountability for its investment of public funds,”<sup>136</sup> the statute itself does not explicitly mandate that the tool be publicly accessible.<sup>137</sup> While the RePORT tools provide insight into many elements of NIH-funded research, they do not reveal the detailed clinical trial cost information discussed in Section IV.<sup>138</sup>

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<sup>132</sup> See Jennifer Miller, Joseph S. Ross, Marc Wilenzick, Michelle M. Mello, *Sharing of clinical trial data and results reporting practices among large pharmaceutical companies: cross sectional descriptive study and pilot of a tool to improve company practices*, *BMJ* (Jul. 10, 2019), <https://www.bmj.com/content/366/bmj.l4217.long>. Among trials of FDA-approved drugs sponsored by drug companies, ‘a median of 100% (interquartile range 91-100%) of patient trials per drug were registered’ on ClinicalTrials.gov, even as only ‘65% (36-96%) reported results or provided a clinical study report (CSR) summary, and 45% (30-84%) were published.’

<sup>133</sup> See *supra* note 31.

<sup>134</sup> 42 U.S.C. § 282B.

<sup>135</sup> See *Biennial Report of the Director National Institutes of Health Fiscal Years 2008 & 2009: Improving Research Management*, <https://report.nih.gov/biennialreport0809/ViewSection.aspx?sid=61&cid=1> (last accessed March 30, 2020) (describing the creation of RePORT in connection with the Congressional mandate in the NIH Reform act to “build a tool to categorize the agency’s research”).

<sup>136</sup> See *Biennial Report of the Director National Institutes of Health Fiscal Years 2008 & 2009: Improving Research Management*, <https://report.nih.gov/biennialreport0809/ViewSection.aspx?sid=61&cid=1> (last accessed March 30, 2020).

<sup>137</sup> See 42 U.S.C. § 282B (“The Secretary, acting through the Director of NIH, shall establish an electronic system to uniformly code research grants and activities of the Office of the Director and of all the national research institutes and national centers. The electronic system shall be searchable by a variety of codes, such as the type of research grant, the research entity managing the grant, and the public health area of interest. When permissible, the Secretary, acting through the Director of NIH, shall provide information on relevant literature and patents that are associated with research activities of the National Institutes of Health.”).

<sup>138</sup> Some projects have a breakdown of “direct” and “indirect” costs. While this is a step in the right direction, it is not the robust data set discussed in Section IV, *supra*, and is not enough to scrutinize actual costs.



## 1. RePORTER

The RePORT Expenditures and Results module (“RePORTER”) allows the public to access a variety of data points related to NIH-funded research, including both extramural and (at least some) intramural research.<sup>139</sup> While much of this data can be useful for investigating the R&D costs of developing a particular drug, it does not provide a clear picture of clinical trial costs, due to the difficulty of connecting particular clinical trials with specific grants and the lack of disaggregated cost data.

Users seeking information about a known project can query the database by Project Number or Application ID. Alternately, users can search for projects by a variety of terms including the Principal Investigator, the Organization, and a Text Search.

Once a user submits a query, a list of results is returned on a Search Results page. Tabs on the Search Results page allow users to view publications, patents, clinical studies, data and visualizations, and maps for all results.

To find more information about a particular project, users can click the project name to open a Project Information page. The Project Information page has tabs for the project description, details, results, history, subprojects, clinical studies, similar projects, and nearby projects.

This page provides basic project information such as the principal investigator, awardee organization, and an abstract text which describes the project. On the project details tab, additional information is provided, including project funding information for the year of the award, sometimes divided into direct and indirect costs.

The Project Information page also provides publications associated with the grant (which sometimes cite a clinical trial’s NCT number) and patents, both on the Results tab, along with clinical trials on the Clinical Studies tab (more on this below).

While RePORTER provides a wealth of useful data, it does not provide a clear assessment of clinical trial costs. First, while users can query reports associated with a particular clinical trial by entering a ClinicalTrials.gov ID number (NCT number) on the query page, the results identified may not have a one-to-one relationship with the clinical trial being researched. This can occur when a funded research project, such as

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<sup>139</sup> Query Form, NIH RePORT, <https://projectreporter.nih.gov/reporter.cfm>. For information on how to use the tool, see RePORTER Manual, [https://projectreporter.nih.gov/RePORTER\\_Manual\\_files/RePORTERManual.pdf](https://projectreporter.nih.gov/RePORTER_Manual_files/RePORTERManual.pdf) (last accessed March 22, 2020).



a bio-specimen bank, supports multiple clinical trials. For instance, Project A might be identified through a search on Clinical Trial Z, but Project A might actually be associated with multiple clinical trials (Clinical Trials X, Y, and Z), making it difficult to disaggregate which funding was used for which trial.<sup>140</sup>

Next, when users do not enter a particular clinical trial number (NCT number) into the query form, the clinical trials listed on the Clinical Studies tabs might not even be related to the project a user is viewing. For large, multi-project grants (divided between a parent project and subprojects) the Clinical Studies tab appears to list any clinical trials that are associated with either the parent project or any subproject.<sup>141</sup> These sub-projects could focus on different conditions than the conditions queried. As the disclaimer on the webpage explains, “[i]f you performed a search for grants related to breast cancer, there will be grants in the RePORTER hit list supporting research on treatments for breast cancer, but these same grants may be supporting clinical studies of treatments for other types of cancer too. . . . For a more complete and accurate search of all clinical studies (including those that don't cite NIH-funded projects), please visit [clinicaltrials.gov](https://clinicaltrials.gov).”<sup>142</sup>

Additionally, there is unclear linkage between NIH-funded clinical trials, as identified by searching based on funder type on ClinicalTrials.gov,<sup>143</sup> and projects on RePORTER. For instance, ClinicalTrials.gov lists the Ebola Virus Disease Survivors: Clinical and Immunologic Follow-up trial as sponsored by the National Institute of Allergy and Infectious Diseases (NIAID).<sup>144</sup> A search of the corresponding NCT number (NCT02431923) on RePORTER identifies no results. It is unclear why this is the case, but there does appear to be a report in the intramural database regarding the project.<sup>145</sup>

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<sup>140</sup> For example, a search of RePORTER for the year 2019 and clinical trial NCT01318317 returns eleven sub-projects under the main project 5P50CA107399-12. A search of RePORTER for the same year, but clinical trial NCT01815749 returns exactly the same projects. The projects returned in RePORTER are resources and programs that support multiple clinical trials (such as a career enhancement program, sub-project ID 5666, and a biospecimen bank, sub-project ID 5659).

<sup>141</sup> See RePORTER User Manual, *supra* note 139 at 33.

<sup>142</sup> Search Results, [https://projectreporter.nih.gov/reporter\\_CTResults.cfm?icde=49445122](https://projectreporter.nih.gov/reporter_CTResults.cfm?icde=49445122).

<sup>143</sup> From the Advanced Search page on ClinicalTrials.gov, select a Funder Type of NIH, <https://clinicaltrials.gov/ct2/search/advanced?cond=&term=&cntry=&state=&city=&dist=>.

<sup>144</sup> *Ebola Virus Disease Survivors: Clinical and Immunologic Follow-up*, National Institutes of Health Clinical Center (CC) (National Institute of Allergy and Infectious Diseases (NIAID)) (last updated May 27, 2020), <https://clinicaltrials.gov/ct2/show/NCT02431923>.

<sup>145</sup> H. Clifford Lane, *Pathogenesis, Treatment and Prevention of Emerging Infectious Diseases*, NIH Annual Intramural Research Report, 2019 Fiscal Year (October 01, 2018 - September 30, 2019), <https://intramural.nih.gov/search/searchview.taf?ipid=109625&ts=1585650089>. See Section V.B.2.ii for a further discussion of the intramural database. While there are no NCT numbers associated with the record in the intramural database, so we cannot be certain that the projects are linked, an article listed on the intramural record, *A Longitudinal Study of Ebola Sequelae in Liberia*,



If the data is indeed hosted by the intramural database, this could account for the gaps in data found in RePORTER, as some data in the intramural database is apparently missing from RePORTER. As the RePORTER FAQs note, “The information found in RePORTER is drawn from several extant databases . . . [including] the NIH Intramural Database . . . using linkages among these disparate data sources. The comprehensiveness of these databases varies, as does the quality of the linkages formed among them.”<sup>146</sup>

Finally, even if one could query a list of grants in such a way that provides a clear picture of the overall NIH funding for a particular clinical trial, RePORTER does not provide disaggregation beyond separately listing direct and indirect costs for any given grant. While it is true that the sub-projects for a large grant may provide a helpful window into the breakdown of costs (for instance, by putting precise dollar amounts on funding that went to infrastructure or lab services to support the multi-project grant as a whole), it is not likely to provide every data point we propose in Section IV and will not give insight into all clinical trials, due to lack of standardization.

## 2. Other RePORT Tools

In addition to RePORTER, the NIH maintains a variety of other RePORT tools that have the potential to increase the transparency of clinical trial costs, including the Data Book<sup>147</sup> and the intramural database.<sup>148</sup>

### i. Data Book

The Data Book is a NIH-administered website that provides a graphical representation of “summary statistics on extramural grants and contract awards, grant applications, the organizations that NIH supports, the trainees and fellows supported through NIH programs, and the national biomedical workforce.”<sup>149</sup>

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<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6478393/>, does list the trial and NCT number in the Acknowledgements section.

<sup>146</sup> The FAQ goes on to state, “[o]ver time, the quality of RePORTER data has improved as a result of changes in both data collection (e.g., implementation of the NIH Public Access policy) and the increased ability to identify missing information that comes from making these data accessible to more people.” This indicates perhaps some willingness to continue to improve the quality of the data.

<sup>147</sup> NIH Data Book, <https://report.nih.gov/nihdatabook/> (last accessed March 22, 2020).

<sup>148</sup> NIH intramural database, <https://intramural.nih.gov/search/index.taf>, (last accessed March 22, 2020).

<sup>149</sup> NIH Data Book FAQs, <https://report.nih.gov/nihdatabook/page/faq/1>, (last accessed June 23, 2020).



For instance, Data Book Report ID 158 provides a line chart tracking the average funding of R01 grants (the NIH Research Project Grant Program)<sup>150</sup> in current and constant dollars. While there are currently no graphs reporting cost breakdowns of clinical trials, this tool could potentially host such a report.

## ii. Intramural Database

The intramural database is a separate NIH-administered website that provides annual reports on NIH's intramural projects. The intramural database allows users to search by report year, center, and search terms and retrieve lists of annual reports on intramural research projects. The Research Report page lists information about the project including the Principal Investigator, Research Organization (e.g., NIAID), Collaborators (both intramural and extramural),<sup>151</sup> a project summary, and publications generated, but does not include any funding information.<sup>152</sup>

There are a number of barriers to using the intramural database as a tool to increase the transparency of clinical trial spending. The first and most obvious is the lack of cost reporting for projects in the database.<sup>153</sup> Secondly, while it seems that there are links among projects in the intramural database and projects in NIH's other databases, those associations are not made explicit on the intramural project page. There are currently no NCT numbers listed on intramural project pages, even when the project appears to support a clinical trial. For instance, a publication listed for the intramural project "Pathogenesis, Treatment and Prevention of Emerging Infectious Diseases"<sup>154</sup> suggests that the project is linked to the Ebola Virus Disease Survivors: Clinical and Immunologic Follow-up trial (the earlier-mentioned clinical trial that does not return any results on RePORTER).<sup>155</sup> But the project report itself does not list any associated NCT numbers. Additionally, there is no link to records in RePORTER, even when an association between an intramural project and a RePORTER record exists. Currently, some RePORTER entries do have a link to the "NIDB Annual Report" (the

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<sup>150</sup> *Research Grants*, NIH Grants and Funding, [https://grants.nih.gov/grants/funding/funding\\_program.htm#RSeries](https://grants.nih.gov/grants/funding/funding_program.htm#RSeries), (last accessed June 23, 2020).

<sup>151</sup> For an overview of intramural-extramural collaborations, see *Intramural / Extramural Collaborations*, NIH Office of Intramural Research (Feb. 1, 2015), <https://oir.nih.gov/sourcebook/ethical-conduct/research-ethics/nih-policies/intramural-extramural-collaborations>

<sup>152</sup> See, e.g., *Pathogenesis, Treatment and Prevention of Emerging Infectious Diseases*, NIH Annual Intramural Research Report, 2019 Fiscal Year, <https://intramural.nih.gov/search/searchview.taf?ipid=109625&ts=1585650089>, (last accessed June 23, 2020).

<sup>153</sup> See *id.*

<sup>154</sup> *Id.*

<sup>155</sup> See *supra* note 144.



intramural project page) on the RePORTER Project Description page.<sup>156</sup> The associated intramural projects, however, do not link out to the RePORTER record.

### C. Reports to Congress

The NIH is mandated by statute to provide triennial reports on its research activities to Congress.<sup>157</sup> The FDAAA, which was enacted in 2007 as part of an overall effort to increase transparency in biomedical research,<sup>158</sup> requires reporting by the Director of the following cost- and funding-related information: a description of intra-NIH research activities, including the percentage of funds allocated by each center or institute to research involving collaboration with another institute or center;<sup>159</sup> a review of each entity receiving funding in its capacity as a “center of excellence,” including “an evaluation of the performance and research outcomes of each center of excellence;” and recommendations for improving the effectiveness, efficiency, and outcomes of the centers of excellence,<sup>160</sup> and “dollar amounts obligated” for disease-specific research activities.<sup>161</sup> Lastly, the statute provides that in addition to the mandated reports, “the Director of NIH or the head of a national research institute or national center may submit to the Congress such additional reports as the Director or the head of such institute or center determines to be appropriate.”<sup>162</sup>

The NIH has chosen to submit biennial rather than triennial reports to Congress.<sup>163</sup> All reports since 2007, when the reporting requirement was passed, are available on the NIH’s website; however, this public posting does not appear to be required by statute.<sup>164</sup> The NIH is not required to nor does it report disaggregated costs of specific clinical trials, but the catch-all provision in the triennial report statute, noted

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<sup>156</sup> See, e.g., *1ZIACP000101-15 Project Information*, NIH RePORT, [https://projectreporter.nih.gov/project\\_info\\_description.cfm?aid=10007390&icde=49462391](https://projectreporter.nih.gov/project_info_description.cfm?aid=10007390&icde=49462391) (last accessed June 24, 2020), which links to the NIDB Annual Report. *Human Studies of Diet and Nutrition*, NIH Annual Intramural Research Report, <https://intramural.nih.gov/search/searchview.taf?ipid=108958&ts=1586000369> (last accessed June 24, 2020).

<sup>157</sup> 42 U.S.C. § 283.

<sup>158</sup> See Andrew C. von Eschenbach, *The FDA Amendments Act: Reauthorization of the FDA*, 63 FOOD & DRUG L. J. 579, 581 (2008) (describing FDAAA as “massive legislation” informed by a “spirit of transparency”).

<sup>159</sup> 42 U.S.C. § 283(a)(3)(A).

<sup>160</sup> *Id.* at § 283(a)(6)(A-B).

<sup>161</sup> *Id.* at § 283(b)(2).

<sup>162</sup> *Id.* at § 283(c).

<sup>163</sup> *NIH Triennial [sic] Report*, Office of Evaluation, Performance, and Reporting (last updated March 18, 2019), <https://dpcpsi.nih.gov/oepr/nih-biennial-report>.

<sup>164</sup> *Biennial Report of the Director, National Institutes of Health Fiscal Years 2014 & 2015* (Jun. 13, 2018), <https://report.nih.gov/biennialreport/>.



above, suggests that the Director has the power to impose this additional reporting requirement on the NIH.

The NIH is further required by statute to develop and submit to Congress and publicize, at least every six years, a coordinated strategy known as the “NIH Strategic Plan.”<sup>165</sup> The Strategic Plan must identify and prioritize short-term and long-term research needs and “include strategic priorities for funding research through the Common Fund.”<sup>166</sup> The Common Fund is a certain percentage of dollars appropriated to the NIH by Congress which is set aside for “identify[ing] research that represents important areas of emerging scientific opportunities, rising public health challenges, or knowledge gaps that deserve special emphasis and would benefit from conducting or supporting additional research that involves collaboration between 2 or more national research institutes or national centers, or would otherwise benefit from strategic coordination and planning.”<sup>167</sup> The plan must include certain funding estimates by the Director.<sup>168</sup>

Additionally, 42 U.S.C. § 241 describes the authorities of the Secretary of the Department of Health and Human Services (HHS) relating to research activities, which includes any research conducted or funded by the NIH. The Secretary is permitted to “collect and make available through publications and other appropriate means, information as to, and the practical application of, such research and other activities.”<sup>169</sup> This broad authorization suggests that the Secretary may direct the NIH to collect and publish detailed information regarding the costs of clinical trials funded by the NIH.

The Institutes and Centers of the NIH also provide various quantities of relatively high-level summary information regarding their activities, spending, and successes. The Clinical Center, for instance, provides an annual data report that includes information on clinical research activity.<sup>170</sup> This gives an overall summary of the number of protocols at the Center, broken down by clinical trial phase, budgeting by major category (salaries and benefits, medications, contracts by labor and non-labor, assessments, supplies, equipment, and all other),<sup>171</sup> and patient activity (by admissions, new patients, inpatient days, average length of stay, and outpatient visits).<sup>172</sup>

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<sup>165</sup> 42 U.S.C. § 282(m).

<sup>166</sup> *Id.* at § 282(m)(2)(D).

<sup>167</sup> *Id.* at § 282(b)(7)(A)(i).

<sup>168</sup> *Id.* at § 282(c)(1)(C).

<sup>169</sup> *Id.* at § 241(a)(1).

<sup>170</sup> *NIH Clinical Center Data Report 2019: Report on 2018 Activities* (2019), <https://clinicalcenter.nih.gov/about/pdf/2019CCDataReport.pdf>.

<sup>171</sup> *Id.* at 5.

<sup>172</sup> *Id.*



## D. Freedom of Information Act

The Freedom of Information Act (FOIA) allows members of the public to request records from any federal agency.<sup>173</sup> Under FOIA, a federal agency must generally make information—“records”—within its possession “promptly available” to “any person”<sup>174</sup> who requests that information.<sup>175</sup> The NIH has a FOIA office that handles and fulfills hundreds of FOIA requests per year.<sup>176</sup> However, the NIH does not fulfill all FOIA requests for clinical trial cost information. Under FOIA, federal agencies may invoke one or more of nine distinct exemptions to withhold information from the requester. Federal agencies may also withhold information from requesters if that information has not already been memorialized in a digital or paper “record” at the time of the FOIA request.<sup>177</sup> In the past, NIH has fulfilled some FOIA requests for clinical trial cost data but has refused to fulfill others, invoking the FOIA exemptions and/or alleging that the NIH does not maintain existing “records” of intramural trial costs of the sort required to be disclosed under FOIA.<sup>178</sup>

A pervasive feature of FOIA—even when it works—is that it is primarily reactive and slow: FOIA requires a requester to know what information she seeks before she

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<sup>173</sup> *FOIA.gov*, U.S. Dept. of Justice (last accessed June 24, 2020), <https://www.foia.gov/about.html>.

<sup>174</sup> For purposes of making a FOIA request, a “person” can be any individual or organization, commercial or noncommercial, citizen or noncitizen, located anywhere in the world. See 1 West’s Fed. Admin. Prac. § 709 (“Freedom of Information Act—Procedure for requests”).

<sup>175</sup> 5 U.S.C. § 552.

<sup>176</sup> *HHS Fiscal Year 2019 Freedom of Information Annual Report*, U.S Dept. of Health and Human Services, <https://www.hhs.gov/foia/reports/annual-reports/2019/index.html>, (last accessed June 24, 2020).

<sup>177</sup> See *Dep’t of Justice v. Tax Analysts*, 492 U.S. 136, 144-145 (1989) (defining a “record” for purposes of FOIA to require that the requested information has already been “create[d] or obtain[ed]” by an agency and is within the agency’s control “at the time the FOIA request is made”).

<sup>178</sup> Researchers at Knowledge Ecology International (KEI) generously shared some of their FOIA experience at the NIH with the authors. KEI has filed numerous FOIA requests seeking disaggregated cost data from clinical trials. See, e.g., NIH FOIA Request Nos. 46238, 47571, 52838, 52847, and 53570. These requests sought broadly similar types of cost data but received disparate responses from NIH. For example, NIH disclosed only minimal information in response to Request No. 47571, which sought information on the budgets of clinical trials funded by NIH for chimeric antigen receptor T-Cell (CAR T-Cell) therapies, but disclosed detailed information on the budget and design of an NIH-funded trial conducted at Baylor University Medical Center, NCT01189383 (“IL15 Dendritic Cell Vaccine for Patients With Resected Stage III (A, B or C) or Stage IV Melanoma”), in response to Request No. 53570. In other instances, the NIH FOIA office has declined to fulfill FOIA requests from KEI for disaggregated data on the costs of clinical trials run through NIH’s intramural program on the basis that the NIH does not maintain regular records of such data. Details of these requests are on file with the editor of this white paper.



asks, to formulate a request precisely and narrowly,<sup>179</sup> and then to wait until the request is fulfilled. At NIH, the wait is usually months, and sometimes years.<sup>180</sup> If NIH (or any federal agency) denies a FOIA request or fails to fulfill it promptly, the requester can go to federal court to challenge the agency,<sup>181</sup> but litigation in federal court is typically slow and resource-intensive.

## VI. OPTIONS FOR REFORM AND TOP RECOMMENDATIONS

In this section, we lay out recommended reforms and how to achieve them. While each existing type of disclosure discussed in Section V could be improved to report more cost data, only changes to ClinicalTrials.gov and RePORTER could fully accomplish the goals laid out in Sections III and IV.

Our primary recommendation is that U.S. federal statutory law be changed to require all trial sponsors that receive NIH funding – industry, universities, and NIH itself – to report disaggregated clinical trial cost data on a per-trial basis on ClinicalTrials.gov. We propose amending the ClinicalTrials.gov database to include an additional “Costs” section in the existing “Study Details” page for any clinical trial entry. Upon study completion, sponsors of NIH-funded trials would be required to submit cost data to the NIH along with the clinical trial results currently required by statute and the associated rule for publication on ClinicalTrials.gov. As with existing ClinicalTrials.gov reporting requirements (over which the NIH shares enforcement responsibility with the FDA), NIH would be responsible for ensuring compliance with this new obligation.

A next-best, or perhaps complementary, reform would be changes to RePORTER, as outlined below. We also briefly describe other reforms that could increase the availability of cost data, but these should be prioritized below changes to ClinicalTrials.gov and RePORTER, as they may not fully accomplish the objectives laid out in Section IV.

Before discussing these options for reform, we note a key prerequisite: the NIH must keep records of its own spending on intramural clinical trials. It seems fair to assume that, though RePORTER only displays lump sum grant awards, the NIH tracks disaggregated costs of extramural research, given the extensive trial-by-trial cost

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<sup>179</sup> Christopher J. Morten & Amy Kapczynski, *The Big Data Regulator, Rebooted: Why and How the FDA Can and Should Disclose Confidential Data on Prescription Drugs*, 109 CALIF. L. REV. \_\_\_ (forthcoming 2021).

<sup>180</sup> *FOIA Annual Report 2019*, *supra* note 176.

<sup>181</sup> See Morten & Kapczynski, *supra* note 179.



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estimate reporting required of many grantees.<sup>182</sup> While RePORTER currently contains some entries for intramural research projects with associated funding awards, it is unclear to what extent intramural programs track disaggregated spending to the same level of detail. For any of the following recommendations to be implemented fully, the first step must be for NIH to maintain uniform records of its spending on its own intramural research.

#### A. ClinicalTrials.gov

##### 1. Recommendation: Disclose Clinical Trial Costs on ClinicalTrials.gov

ClinicalTrials.gov is the ideal place for the NIH to report data on the costs of clinical trials. As discussed in Section V, ClinicalTrials.gov is a comprehensive database for the registration of clinical trials and the publication of clinical trial information and results. The website is structured to collect and display detailed information about every registered study, and only small changes would be necessary to include cost data. Cost reporting on the extant “Study Details” page for clinical trials on ClinicalTrials.gov would best achieve the goals set out in Section IV. Although the focus of this paper is increased transparency for NIH-funded trials, if ClinicalTrials.gov were revised to permit submission and publication of trial cost data, then other trials not funded by NIH could also be encouraged or required to report trial costs to ClinicalTrials.gov.

Ideally, the full set of data points in Section IV would be listed in a Costs section on ClinicalTrials.gov for each clinical trial that received NIH funding. While the data points proposed in Section IV would provide the most comprehensive data set for calculating total costs of R&D for any given drug, any level of cost data disclosure on ClinicalTrials.gov would be an improvement to the current system. A second-best option would be to require less detailed cost reporting, such as overall trial cost per patient, per year. Finally, while not ideal, the NIH could simply report on ClinicalTrials.gov a single data point for each clinical trial it funds or sponsors: the overall trial cost.

As we explain further below, we recommend using ClinicalTrials.gov to publish the costs associated with individual clinical trials because the ClinicalTrials.gov database is organized by trial, which creates a clear connection between the cost data and a specific clinical trial. This feature of ClinicalTrials.gov makes it more useful than RePORTER, as the RePORTER database is organized by grant rather than by trial, and it can be difficult to connect data with a specific clinical trial.

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<sup>182</sup> See *supra* Section IV (describing the reporting requirements for NIH grantees).



## 2. Three Ways—Legislative, Administrative, and Executive—to Require Disclosure of Clinical Trial Costs on ClinicalTrials.gov

The best way to achieve disaggregated cost reporting on ClinicalTrials.gov is to amend the statute governing ClinicalTrials.gov, 42 U.S.C. § 282(j). Though statutory reform may be a lengthier and more difficult process than agency rulemaking or policymaking, for that same reason, the reform is likely to be more permanent. Given FDAAA’s multiple lists of statutorily-required data and emphasis on making clinical trial data available to the public,<sup>183</sup> an amendment requiring NIH to collect and disclose the recommended data points would be consistent with the overall purpose and structure of the statute.

The next best option would be a statutory amendment to § 282(j) requiring NIH to disclose clinical trial costs without specifying the particular breakdown of costs. Lastly, if statutory amendments are not possible, disclosure of clinical trial costs on ClinicalTrials.gov could also be achieved through administrative or executive action, as explained below. While less appealing in the sense that administrative or executive action would be less permanent than statutory change, administrative or executive action could be undertaken at any time and would be simpler and quicker than a statutory amendment.

### i. Legislative Action: Amend 42 U.S.C. § 282(j)

Under 42 U.S.C. § 282(j), responsible parties are required to register applicable clinical trials on ClinicalTrials.gov and report certain basic and expanded trial results. The statute defines a long list of trial result data points required to be reported and disclosed and instructs the Secretary of HHS to define further reporting requirements.<sup>184</sup> Congress could amend the statute in a few ways to require specific cost reporting.

This statutory amendment could impose two distinct obligations, one on NIH’s grantees and one on NIH itself: (1) it could require any trial sponsor who receives funding from the NIH to report its cost breakdown to NIH upon trial completion, for publication on ClinicalTrials.gov, and (2) it could place the burden entirely on the NIH to disclose any cost information NIH possesses, whether related to its own spending or that of its grantees. Ideally, the statute should require both. The first obligation is necessary to obtain a full picture of clinical trial costs because many NIH grantees also

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<sup>183</sup> See Andrew C. von Eschenbach, *The FDA Amendments Act: Reauthorization of the FDA*, 63 FOOD & DRUG L. J. 579, 581 (2008) (describing FDAAA as “massive legislation” informed by a “spirit of transparency”).

<sup>184</sup> 42 U.S.C. § 282(j)(3)(C-D).



possess other sources of funding.<sup>185</sup> On the other hand, it could be counterproductive for the NIH to rely on grantees to submit cost data that it possesses, in part because responsible parties may sometimes fail to submit complete, accurate, and timely cost data. Thus, the second obligation would act as a valuable fallback, ensuring that the NIH discloses on ClinicalTrials.gov at least the cost data it receives from grantees, even if trial sponsors do not report any cost information themselves.

To impose these obligations, Congress should first amend the subsection titled “NIH information,” § 282(j)(3)(A)(ii)(II), to require the NIH to report any information on clinical trial costs that it possesses. This would include the entire cost of an intramural clinical trial as well as any information the NIH receives from grantees conducting extramural research, even if those extramural clinical trials also use other sources of funding.

Second, Congress should also amend § 282(j) to require all clinical trial sponsors who receive any NIH funding to report all costs of those clinical trials. This requirement could be incorporated into the existing statute in at least three distinct ways. First, Congress could add a cost reporting requirement to the required elements of basic results in § 282(j)(3)(C), which already mandates reporting of specific clinical trial information. Second, Congress could add cost reporting to the required elements of expanded results required by § 282(j)(3)(D)(iii).<sup>186</sup> Lastly, Congress could create an entirely new sub-paragraph to § 282(j) that applies only to clinical trials funded in whole or in part by the NIH and requires cost reporting. In all scenarios, the statute should be amended to mandate reporting of the specific data points discussed in Section IV.

Congress could alternatively amend the statute to require cost reporting but delegate the definition of specific data points to the Secretary of HHS and/or the Director of the NIH. This provision could explicitly create a new delegation of authority under which the Director of the NIH must promulgate a rule defining the disaggregated data points to be reported, and then instruct NIH to promulgate that rule by some date. Alternatively, the provision could instruct NIH to promulgate a rule under any one of the multiple existing delegations of authority to the Secretary of HHS to define the scope of

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<sup>185</sup> A 4/30/2020 search of ClinicalTrials.gov for all clinical trials with a funder type of both “NIH” and “Industry” revealed 2089 results. These results were produced by running the following query through the “expert search:” “AREA[FunderTypeSearch] EXPAND[Term] COVER[FullMatch] ( "NIH" AND "INDUSTRY" )”. The “expert search” is available here: [https://www.clinicaltrials.gov/ct2/results/refine?show\\_xprt=Y](https://www.clinicaltrials.gov/ct2/results/refine?show_xprt=Y).

<sup>186</sup> Since both the basic results and the expanded results provisions apply to all responsible parties, not only those who receive grant money from NIH, amendments to these sections could impose cost reporting requirements on all responsible parties, not just NIH grantees, unless the amendment specified that cost reporting is only required for NIH-funded clinical trials.



information disclosed on ClinicalTrials.gov. While this proposal in theory could result in the same disclosures as a statutory amendment detailing the required data points, it is suboptimal for two reasons: (1) it leaves the initial definition of specific data points to the discretion of the Director of the NIH and (2) it would be easier for a future NIH Director to redefine data points by promulgating a new rule than it would be for Congress to repeal or amend the statute.

ii. Administrative Action: Promulgate a Rule or Amend Policy

While we recommend statutory changes over agency rules, the NIH can promulgate a rule without any statutory amendments, and an NIH rule requiring the reporting of disaggregated costs for any clinical trial that receives NIH funding would accomplish the goals laid out in this paper. As discussed above, statutory amendment is our top recommendation because it is more permanent and would ensure that sharing of clinical trial cost data remains the law in the event of a leadership change at NIH. But an agency rule might be faster and easier to enact in the first instance.

We believe the NIH already has the authority to promulgate a rule requiring this reporting without additional Congressional action. The statutory provision mandating ClinicalTrials.gov contains two separate delegations of authority to the Secretary of HHS and, by proxy, the Director of NIH to define additional reporting requirements.<sup>187</sup> The NIH could promulgate a new rule defining expanded results to include detailed cost reporting or amend its existing relevant rule, the FDAAA Final Rule, “Clinical Trials Registration and Results Information Submission.”<sup>188</sup>

The NIH could also amend its existing “Policy on the Dissemination of NIH-Funded Clinical Trial Information,” which requires sponsors of any clinical trials funded in whole or in part by the NIH to register their clinical trials and report results, regardless of whether the clinical trials are required to be registered by statute.<sup>189</sup> This policy, which notes that “transparency will improve future research designs and maximize the public's investment—and their trust—in research,” can be amended by the NIH to include a cost reporting requirement for all clinical trials that receive NIH funding.

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<sup>187</sup> See 42 U.S.C. § 282(j)(3)(D)(i) (“To provide more complete results information and to enhance patient access to and understanding of the results of clinical trials, not later than 3 years after the date of the enactment of the Food and Drug Administration Amendments Act of 2007 [enacted Sep. 27, 2007], the Secretary shall by regulation expand the registry and results data bank as provided under this subparagraph.”); § 282(j)(3)(D)(iii)(IV) (“The regulations under this subparagraph shall require, in addition to the elements described in subparagraph (C), information within each of the following categories:.... (IV) Such other categories as the Secretary determines appropriate.”).

<sup>188</sup> 42 C.F.R. § 11.48.

<sup>189</sup> *NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information*, NIH Grants and Funding (Effective Jan. 18, 2017), <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-149.html>.



### iii. Executive Action: Issue an Executive Order, Presidential Memorandum, or Proclamation

The NIH is subject to executive action by the President of the United States.<sup>190</sup> An Executive Order, Presidential Memorandum, or Proclamation<sup>191</sup> can direct the NIH to enact the recommended changes to ClinicalTrials.gov.<sup>192</sup> Indeed, the Obama administration used a Presidential Memorandum to increase the transparency of federal agencies,<sup>193</sup> prompting HHS to publish four Open Government Plans between 2010 and 2016.<sup>194</sup> Like administrative action, executive action *could* accomplish the goals of disaggregated clinical trial cost disclosure, but is not the best avenue to achieve lasting reform because any action taken by the executive can be revised or undone by the next administration.

## B. RePORTER

### 1. Recommendation: Disclose Clinical Trial Costs on RePORTER

Though cost reporting in ClinicalTrials.gov is the single best way to accomplish the goals laid out in this paper, implementing certain changes to RePORTER is a second-best option. Because RePORTER has some useful features not found in ClinicalTrials.gov, both the improvements to ClinicalTrials.gov and the following recommendations for RePORTER should be implemented to provide the most transparency into the costs of clinical trials run and funded by NIH.

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<sup>190</sup> See, e.g., *Sherley v. Sebelius*, 689 F.3d 776, 784 (D.C. Cir. 2012) (“NIH may not simply disregard an Executive Order. To the contrary, as an agency under the direction of the executive branch, it must implement the President’s policy directives to the extent permitted by law.”).

<sup>191</sup> There is no clear delineation between these devices. See Todd Garvey, Cong. Research Serv., RS20846, *Executive Orders: Issuance, Modification, and Revocation 2* (2016) (“The distinction between these instruments—executive orders, presidential memoranda, and proclamations—seems to be more a matter of form than of substance, given that all three may be employed to direct and govern the actions of government officials and agencies. Moreover, if issued under a legitimate claim of authority and made public, a presidential directive could have the force and effect of law, ‘of which all courts are bound to take notice, and to which all courts are bound to give effect.’ The only technical difference is that executive orders must be published in the Federal Register, while presidential memoranda and proclamations are published only when the President determines that they have ‘general applicability and legal effect.’”).

<sup>192</sup> See *id.* (noting that EOs, presidential memoranda, and proclamations “may be employed to direct and govern the actions of government officials and agencies.”).

<sup>193</sup> John P. Holdren, Peter Orszag and Paul F. Prouty, *Memorandum for Heads of Departments and Agencies on President’s Memorandum on Transparency and Open Government - Interagency Collaboration*, WhiteHouse.gov (Feb. 24, 2009), <https://www.whitehouse.gov/sites/whitehouse.gov/files/omb/memoranda/2009/m09-12.pdf>.

<sup>194</sup> *Open Government at HHS website*, Immediate Office of the Secretary, <https://www.hhs.gov/open/index.html> (last accessed Feb. 16, 2017).



Overall, the data structure of RePORTER may make it difficult for the tool to become the ultimate provider of disaggregated clinical trial costs, but we recommend two improvements that would make it a more useful source of cost data: (1) a clearer connection between clinical trials and RePORTER records, and (2) further disaggregated cost information.

To achieve a clearer connection between clinical trials and the grants listed in RePORTER, the NIH should limit each grant to funding one single clinical trial, rather than the current structure where one grant can support multiple trials. This would produce a one-to-many data structure in which one clinical trial might be supported by multiple grants, but 100% of the funds from each grant support just that clinical trial. This means that, to calculate total NIH funding for a particular clinical trial, one would simply add up the associated grant funding.

We recognize that this reform to the grant award system may be difficult to implement or even inadvisable for reasons beyond the scope of this paper. In that case, the NIH should require the recipients of grants that support multiple clinical trials to report to the NIH what percentage of the grant's funds support each clinical trial. NIH could then publish this data in RePORTER. This would allow RePORTER users to tally up costs for a single clinical trial across many grants that support many clinical trials.

Second, RePORTER should be more granular in its cost breakdown. As discussed in Section VII, there is strong reason to believe that NIH's awardees submit a breakdown of costs by personnel costs, equipment, travel, training, materials and direct supplies, publication costs, consultant services, data processing, sub-awards, equipment and/or facility rental fees, and alterations and renovations costs. If NIH collects this data, it should retain and disclose it.

While these two reforms to RePORTER would go a long way toward providing disaggregated cost information for clinical trials, some barriers might still exist. For instance, when a user views a particular grant, RePORTER may remain unclear as to whether that grant is the only funding for an associated clinical trial, or whether there are other sources of funding for that trial. Overall, the ideal first stop for disaggregated clinical trial cost information remains ClinicalTrials.gov, where users could see all funding associated with the trial in one place.

Further, in order to fully accomplish the goals laid out in Section IV, both of the changes proposed in this section— (1) clarity into the relationship between grants and



clinical trials and (2) disaggregated cost reporting—would be necessary to make RePORTER a comprehensive source for clinical trial cost reporting.

## 2. Two Ways—Legislative and Administrative—to Require Disclosure of Clinical Trial Costs on RePORTER

### i. Legislative Action

#### a. Mandate that RePORT Be Public

First, while RePORT (the NIH’s collection of online tools, which includes RePORTER) is currently publicly available and the NIH seems to have interpreted 42 U.S.C. § 282b to require this,<sup>195</sup> the statutory text itself does not appear to mandate this result.<sup>196</sup> To ensure that NIH continues to make RePORTER publicly available, we recommend that section 282b be amended to require expressly that the RePORTER electronic system be “publicly available” or “accessible by the public.”<sup>197</sup>

#### b. Clarify Connections Between Clinical Trials and Grants

Congress should amend Title 42 of the U.S. Code to require the NIH to clarify the connection between grants made through its extramural research program and individual clinical trials. One option would be amending the statute to only allow a given grant to be associated with a single clinical trial (while still allowing a single clinical trial to be associated with multiple grants). A logical place for such an amendment would be section 284(b), which authorizes the NIH to issue grants<sup>198</sup> and establishes a peer review process for such grants.<sup>199</sup> Other sections of the code might also be appropriate

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<sup>195</sup> The loading page for search results on RePORTER, for instance, states “Did You Know? RePORTER satisfies a legislative mandate included in the NIH Reform Act of 2006 *to provide the public* with an electronic system to search NIH research projects using a variety of codes, including public health area of interest, and provide information on publications and patents resulting from NIH-funded research.” (emphasis added). *Query Form*, NIH RePORT (last accessed June 24, 2020), <https://projectreporter.nih.gov/reporter.cfm> (to view loading page, submit a query).

<sup>196</sup> 42 U.S.C. § 282b (“The Secretary, acting through the Director of NIH, shall establish an electronic system to uniformly code research grants and activities of the Office of the Director and of all the national research institutes and national centers. The electronic system shall be searchable by a variety of codes, such as the type of research grant, the research entity managing the grant, and the public health area of interest. When permissible, the Secretary, acting through the Director of NIH, shall provide information on relevant literature and patents that are associated with research activities of the National Institutes of Health.”).

<sup>197</sup> If the NIH were to change its position on this and remove the database from public access, it would likely face challenges under the Administrative Procedure Act. However, the best way to ensure that the database remains public is to provide clear statutory language mandating the database be public.

<sup>198</sup> 42 U.S.C. § 284(b)(2).

<sup>199</sup> 42 U.S.C. § 284(b)(3).



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for such a mandate, such as section 284k, which requires the NIH to “support and expand the involvement of the National Institutes of Health in clinical research.”<sup>200</sup>

### c. Require Disaggregated Cost Information

Next, as discussed above in the context of ClinicalTrials.gov, Congress could mandate that disaggregated cost information be disclosed through RePORTER by amending 42 U.S.C. § 282b. The bill could list specific data points, as discussed in Section IV, or amend the statute to require cost reporting but delegate the definition of specific data points to the Secretary of HHS and/or the Director of the NIH.

#### ii. Administrative Action: Promulgate a Rule

Although Congress could mandate the improvements to RePORTER discussed above, we believe the NIH already has discretionary authority to execute these changes under 42 U.S.C. § 282b without additional Congressional action. Costs are already reported for individual grants, including some level of disaggregation, suggesting that passing a rule formalizing the reporting of cost information is well within the NIH’s authority. As discussed above, while agency action may be faster and easier to enact in the first instance, statutory amendments are preferable because they are less subject to change.

The NIH could promulgate a rule requiring each grant to fund only one clinical trial, or in the alternative requiring grantees to report what percentage of the grant funds each associated clinical trial, as discussed *supra*, or requiring the reporting of disaggregated cost information for grants that support clinical trials in RePORTER.

### C. Other Avenues for Reform

While ClinicalTrials.gov is the most suitable option for reform, followed by changes to RePORTER, the following suggestions have the potential to provide some information on the NIH’s clinical trial costs. These avenues, however, are unlikely to achieve comprehensive reporting of disaggregated cost data across all NIH-funded clinical trials.

#### 1. Data Book

The Data Book is a tool administered by the NIH that provides graphical representation of funding data. Because the structure seems designed to present large

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<sup>200</sup> 42 U.S.C. § 284k.



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amounts of data in simple ways, it is not a useful way to present disaggregated per-trial costs. A report in the Data Book could collate data related to the cost of clinical trials. To make the Data Book a useful source, we recommend the following reports be made available:

- Average Clinical Trial Cost by Phase and Therapeutic Area
- Average Clinical Trial Cost by Phase and Institute or Center
- Disaggregated Clinical Trial Costs for Particular Therapeutic Areas or Diseases

It does not appear that the NIH has promulgated a rule regarding the NIH Data Book but instead that the Data Book was created through informal policy. The NIH could likely create the recommended report as a matter of policy as well.

While the suggested reports would provide useful insight into clinical trial spending, it is not the ideal vehicle for reform because it only accounts for extramural research activities and because the reports proposed do not provide a breakdown of costs by each clinical trial.

## 2. NIH Intramural Database

### i. Recommendation: Improve Reporting in the NIH Intramural Database

While changes to the NIH intramural database alone will not achieve the goals of this white paper, some immediate improvements to the intramural database could help overcome the barriers to using the database as a tool to increase the transparency of clinical trials funding.

First, each report in the NIH intramural database could list any linkages between the intramural project and specific clinical trial or trials (through the NCT number). Ideally, the intramural report would both include related clinical trials and allow users to search the database by NCT number. While such a system might run into the concerns presently raised by RePORTER (perhaps some intramural projects support more than one clinical trial), it would be a step in the right direction.

To the extent that intramural research, clinical or otherwise, does not have a corresponding record in RePORTER, such records should be created.

Second, each intramural report should include links to the corresponding RePORTER records, or a notice that there are no corresponding RePORTER records if that is the case. RePORTER is a richer source of information than the intramural database (despite the shortcomings discussed *supra*), insofar as it links to patents,



funding amount, and clinical trials, so users investigating R&D on a particular drug or disease area will benefit more from the RePORTER data. It appears that a link *from* RePORTER *to* the intramural database is already established, as RePORTER has a link to the “NIDB Annual Report” on the Project Description page for certain intramural projects.<sup>201</sup> Our recommended change would simply create a link from the intramural database back to RePORTER.

Finally, the intramural database should report costs and patents associated with the project, data points currently missing from intramural database project reports.

ii. Two Ways – Administrative and Third-Party Litigation – to Achieve Recommended Changes to the Intramural Database

a. Agency Action: Promulgate a Rule or Enact Policy

The NIH, either through rulemaking or through policy, could implement the links to NCT number, RePORTER record, cost reporting, and patent reporting discussed *supra*.

b. Litigation: Potential Third Party Claim Under APA

We note that, due to the statutory language of 42 U.S.C. § 282b and the data gaps that currently exist in RePORTER for intramural projects (as discussed in Section V), there may be the potential to bring an Administrative Procedure Act (APA) claim against the NIH. Section 282b requires the Secretary to “establish an electronic system to uniformly code research grants and activities of the Office of the Director and of all the national research institutes and national centers.”<sup>202</sup> “Research grants” refer to the NIH’s extramural grant funding, while “activities . . . of all the national research institutes and national centers” includes intramural activities. The electronic system is required to “uniformly code” both the extramural grants and intramural activities, and “code” is later expanded upon: “The electronic system shall be searchable by a variety of codes, such as the type of research grant, the research entity managing the grant, and the public health area of interest.”

Thus, there is a credible argument that section 282b requires the inclusion in RePORTER of the same data points for both extramural and intramural projects. An APA lawsuit could be brought in federal district court by an interested third party to compel the NIH to begin disclosing the same data points on intramural research in

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<sup>201</sup> See, e.g., project 1ZIACP000101-15, *supra* note 156.

<sup>202</sup> 42 U.S.C. § 282b.



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RePORTER and the intramural database that NIH is already disclosing on extramural research.

We note that while APA litigation may be an option to increase the availability of data for intramural projects, obtaining this data without the changes we suggest to RePORTER would do little, in practice, to increase the transparency of clinical trials costs because of the shortcomings to RePORTER discussed in Section V.

### 3. Reports to Congress

#### i. Triennial Reports to Congress

##### a. Recommendation: Require Publication and Additional Cost Reporting in Triennial Reports to Congress

The NIH is required by statute to submit a triennial report to Congress on its research activities.<sup>203</sup> The statute lists specific information that the report must contain, including certain aggregated cost information, but it does not require the reporting of any disaggregated clinical trial costs.

We recognize that compiling and reporting costs for all clinical trials completed over the three-year period of the triennial report would be difficult and burdensome for the NIH. Furthermore, triennial reporting would create a significant lag between when trials are completed and when the costs are reported. Instead, we propose a more modest reform to require inclusion in these reports of the total (aggregate) amount spent on clinical trials per fiscal year per disease area. Though this would not accomplish all the transparency goals laid out in this paper, this reform would still convey useful information to the public.

##### b. Two Ways—Legislative and Administrative—to Require Additional Cost Reporting in Triennial Reports

First and foremost, though NIH makes these reports available to the public on its website, there is, to our knowledge, no statutory mandate to make the reports public. Congress should remedy this by codifying a publication requirement in the statute. Secondly, while Congress has specified a long list of the content the triennial report must contain, including certain aggregated cost information, Congress has not mandated disclosure of any disaggregated data. We propose that Congress amend the statute, 42 U.S.C. § 283, to require some disaggregation in addition to the expenditure

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<sup>203</sup> 42 U.S.C. § 283.



reporting that is already required. At minimum, the statute should mandate disclosure of clinical trial costs per fiscal year per disease area.

Secondly, the statute grants discretion to the Director of the NIH as to what data to include in the triennial reports.<sup>204</sup> The NIH therefore has authority to promulgate a rule that clinical trial cost reporting, at any level of disaggregation, be included in the report.

## ii. Institute/Center Annual Reports

As discussed in Section V, individual centers or institutes at the NIH publish regular reports. Thus, there is the possibility that these institutes or centers could publish reports regarding the breakdown of costs associated with the clinical trials they fund. While an individual institute's or center's report may only cover that institute's or center's area of focus, it would be immensely useful for anyone working in that area and could provide a model for other institutes and centers to follow.

There is currently no statute requiring institute- or center-level reporting. Congress could amend Title 42 of the U.S. Code to require a particular institute or center to make annual reports of clinical trial costs. The statute should mandate that the report be publicly available and contain disaggregated, per-trial cost information as recommended in Section IV.

Alternatively, the NIH could promulgate such a rule establishing an annual report for particular centers and institutes through notice and comment rulemaking.<sup>205</sup>

## 4. Freedom of Information Act

Some organizations have had success with using Freedom of Information Act (FOIA) requests to find out disaggregated clinical trial costs; however, some requests have also been met with resistance from the NIH.<sup>206</sup> This remains an avenue for dedicated researchers, but it tends to be slow and resource-consuming, as researchers will have to make requests on a trial-by-trial basis and likely wait months or years for a response.<sup>207</sup> Furthermore, releasing clinical trial cost data through individual FOIA requests is inefficient for the NIH and researchers because responsive information is provided only to the requester. This and other inefficiencies involved in releasing data

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<sup>204</sup> 42 U.S.C. § 283(c) (“[T]he Director of NIH or the head of a national research institute or national center may submit to the Congress such additional reports as the Director or the head of such institute or center determines to be appropriate.”).

<sup>205</sup> *Id.*

<sup>206</sup> See *supra* note 178.

<sup>207</sup> *Id.*



piecemeal to individual requesters make fulfilling FOIA requests a far more expensive process than proactively disclosing cost data. Therefore, although useful, changing FOIA alone is not a viable path to comprehensive reform.

## VII. RESPONSES TO POTENTIAL ARGUMENTS AGAINST R&D COST TRANSPARENCY

This section anticipates and responds to potential arguments against increased R&D data sharing, whether specifically related to costs or other clinical trial data. To our knowledge, there has not been extensive policy debate around increased R&D cost transparency at the NIH. Because of this lack of debate, we are not aware of specific arguments raised against such cost transparency at the NIH. We therefore try to anticipate arguments that may be raised in opposition to the proposals laid out in this paper based on published arguments that the pharmaceutical industry has raised against transparency into its own R&D costs and respond to those.

### A. Argument: The Administrative Burden of Reporting Disaggregated Cost Data Is Too High

Industry groups have opposed efforts to require R&D cost disclosure on the grounds that the administrative cost will be too burdensome. For instance, comments to recently proposed rules on new clinical trial data reporting requirements by industry groups and firms complain that any increased reporting requirements will be time-consuming and expensive.<sup>208</sup> However, cost reporting differs from other data reporting requirements in that it is already internally recorded in the format required for publication. KEI notes, “At present, publicly traded companies already have to disclose information of material interest to investors, and as a consequence of these obligations, many BIO member companies already report outlays on clinical trials.”<sup>209</sup> More broadly, it is unimaginable that any pharmaceutical company, whether privately owned or publicly traded, does not strictly monitor its cash flows.

Applied to the NIH, the concern regarding the proposals described in Section VI is that they will increase administrative burdens on grantees and/or the NIH itself, diverting resources away from the biomedical research at the heart of the NIH’s mission. In this section, we will address this concern from three perspectives: (1) the burden on NIH grantees of reporting more detailed cost information, (2) the costs to the

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<sup>208</sup> *Comment from Laura Hagan, Novartis*, regulations.gov (Mar. 23, 2015), <https://www.regulations.gov/document?D=NIH-2011-0003-0891>; *Comment from Katie McCarthy, BIO*, regulations.gov (Jun. 22, 2009), <https://www.regulations.gov/document?D=NIH-2009-0002-0053>.

<sup>209</sup> James Love, *BIO memo opposing transparency of drug development costs, sales, prices and clinical trial outcomes*, Knowledge Economy International (May 21, 2012), <https://www.keionline.org/21844>.



NIH of collecting and reporting extramural cost information, and (3) the costs to the NIH of tracking and reporting intramural cost information.

### 1. Burden on the NIH's Grantees

We believe that grantees already track many of the data points we recommend they disclose for clinical research funded by extramural research grants from the NIH. The NIH already requires grant recipients to submit progress reports, including the Research Performance Progress Report (RPPR), during and at the end of the award period.<sup>210</sup> The RPPR Instruction Guide, published by the NIH, includes a section on editing the Budget Forms, suggesting that grantees must adjust this information during the project to reflect actual costs.<sup>211</sup> Thus, not only is prospective information collected for extramural grant applications, but there is evidence that costs are updated throughout the project. We recognize that, regardless of the reform pursued, there would likely still be some level of administrative burden. For instance, if the NIH made no changes to RePORTER, but required grantees submit disaggregated clinical trial costs for publication on ClinicalTrials.gov, some grantees might need to begin tracking trial expenses trial-by-trial for grants that currently support multiple clinical trials. However, any additional cost or administrative burden to report costs this way is a miniscule fraction of overall spending by any clinical trial sponsor, and NIH grantees will continue to seek out grants from the NIH even with such a reporting requirement.

As recipients of taxpayer dollars, it is reasonable to expect NIH grantees to track and report how their grant awards are spent. In reference to the burden of additional clinical trial results reporting requirements on NIH grantees, the NIH stated, “[W]e believe that the work should not be seen as a burden, but, rather, an inherent part of an investigator's commitment to the advancement of science.”<sup>212</sup> As explained in Section III, disclosure of clinical trial costs should similarly be viewed as necessary to the advancement of science. Additionally, the NIH offered assistance and additional funding to its grantees to implement the new results reporting requirements and could do so with regard to cost reporting as well.<sup>213</sup>

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<sup>210</sup> *Research Performance Progress Reports (RPPR)*, Electronic Research Administration, Office of Extramural Research (Exp. Date 5/2020), <https://era.nih.gov/grantees/submit-reports/rppr.htm>.

<sup>211</sup> *NIH and Other PHS Agency Research Performance Progress Report (RPPR) Instruction Guide*, Electronic Research Administration, Office of Extramural Research, 34-37 (May 22, 2017), [https://grants.nih.gov/sites/default/files/rppr\\_instruction\\_guide.pdf](https://grants.nih.gov/sites/default/files/rppr_instruction_guide.pdf).

<sup>212</sup> *NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information*, NIH Grants and Funding (Effective Jan. 18, 2017), <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-149.html>.

<sup>213</sup> “We will provide additional guidance to facilitate implementation and help awardees and investigators understand the policy as well as the tasks described in the rule that they will be expected to undertake. In terms of the costs of complying with the policy, grantees are permitted to charge the salaries of administrative and clerical staff as a direct cost. Such staff could assist investigators in meeting their



## 2. Burden on the NIH of Reporting Grantees' Cost Data

Ideally, as described in Section VI, grantees would be required by law to submit disaggregated clinical trial cost data to the NIH along with the trial results required by FDAAA and the FDAAA Final Rule for publication on ClinicalTrials.gov. In this scenario, there would be minimal additional burden to the NIH in publishing that cost data, though NIH would likely need to expend some resources in reviewing the data before publication (as it does with trial results).<sup>214</sup>

However, in the event that the NIH is tasked not just with collecting and publishing cost data submitted by grantees through the ClinicalTrials.gov data submission process, but must in addition create and maintain its own internal records of grantees' spending on extramural clinical trials, the NIH's administrative burden will be greater. Still, the administrative costs will likely be manageable and offset to some degree by potential efficiencies gained by the disclosure. First, much of the administrative burden is placed on grantees, who already report some disaggregated cost data to the NIH through the RPPR process and would, under our proposals, be required to report additional data. The primary burden on NIH would simply be collecting and publishing this data. Though there will be some cost to NIH in changing the reporting mechanism—whether on ClinicalTrials.gov or RePORTER—to allow for the disclosure of additional data points, along with added maintenance costs, these should be minimal. For instance, the databases may need to be updated to contain fields for the new data points, and the user interface may need to be modified. Once the reporting mechanism is established, however, it is likely that the marginal cost of reporting additional data points will be relatively small. Furthermore, the NIH may benefit from the disclosure of this information. First, the NIH currently processes FOIA requests related to the costs of clinical trials<sup>215</sup> and will no longer incur FOIA-related costs if the NIH proactively discloses the information. Second, increased scrutiny of the costs of clinical trials may help the NIH realize efficiencies in its selection and management of grant recipients for extramural clinical trials.<sup>216</sup> On the whole, while the NIH is likely to incur

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responsibilities under the policy. In addition, administrative costs can be covered through indirect cost recovery." *Id.*

<sup>214</sup> Deborah A. Zarin, *et al.*, *Special Report: 10-Year Update on Study Results Submitted to ClinicalTrials.gov*, 381 N. ENGL. J. MED 1966 (Nov. 14, 2019), <https://www.nejm.org/doi/pdf/10.1056/NEJMSr1907644>.

<sup>215</sup> See *supra* note 178.

<sup>216</sup> For example, in its NIH-wide strategic plan for fiscal years 2016-2020, NIH has officially expressed "an increasing interest in fostering approaches to enhance the speed and efficiency with which trials are conducted, as well as to learn more about the role of 'pragmatic trials,' which are trials of direct interest to patients and clinicians." *NIH-Wide Strategic Plan Fiscal Years 2016-2020*, U.S. Dept of Health and Human Services, 17, <https://www.nih.gov/sites/default/files/about-nih/strategic-plan-fy2016-2020-508.pdf>.



some additional administrative costs in reporting this information to the public, these are likely to be offset by future cost savings in other areas. Even if this were not the case, the benefits to public health policy design of having this information decidedly outweigh the administrative costs associated with reporting it.

### 3. Burden on the NIH of Reporting Its Own Intramural Data

Finally, we address potential increased administrative costs to the NIH surrounding disclosure of costs associated with intramural research. First, while we know less about how the NIH tracks its intramural expenditures, if the NIH is not rigorously tracking its own expenditures, it should be. The NIH spends billions of taxpayer dollars per year and should maintain precise records of how it does so. Next, as with requiring the NIH to report extramural cost information, the NIH will likely encounter some additional administrative costs in setting up a reporting mechanism for this data and administering disclosure, but those costs will likely be offset by reduced FOIA requests and increased efficiency of trial selection and design.

#### B. Argument: Disclosure of R&D Costs May Threaten Trade Secrets, Confidential Commercial Information, or the Competitive Position of Drug Developers

Two related possible barriers to clinical trial cost disclosure is that the information constitutes a trade secret or confidential commercial information,<sup>217</sup> and that, as it pertains to industry disclosure of R&D costs, disclosure will harm the competitive position of pharmaceutical companies. For the reasons discussed below, this is not the case.

As an initial matter, costs of intramural research conducted entirely by the NIH, a government agency, cannot be considered trade secrets or confidential commercial information.<sup>218</sup>

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(last accessed June 24, 2020). NIH has also committed to “explore the efficacy of different funding approaches—comparing mechanisms to ascertain their strengths and weaknesses and analyzing whether there is an optimal threshold of funding for research groups via RPG [research project grant] mechanisms.” *Id.* at 36. Making the underlying clinical trial cost data available not only to NIH’s own experts but to experts outside the agency will permit those outside experts to weigh in on these questions and inform NIH’s decision-making.

<sup>217</sup> While there is no universally accepted definition, a trade secret is generally something that has some economic value and has been subject to reasonable precautions to prevent its disclosure. See Rest. 2d of Torts § 757; Uniform State Trade Secrets Act § 1; 18 U.S.C. § 1839(3). Confidential commercial information is a broader category of information protected from disclosure under FOIA. See, e.g., *Department of Justice Guide to the Freedom of Information Act, Exemption 4*, justice.gov, 4, <https://www.justice.gov/oip/page/file/1207891/download> (last accessed June 24, 2020).

<sup>218</sup> David Levine discusses the potential for governmental trade secrets in a 2011 article, *The People’s Trade Secrets?*, and expresses the concern that governmental trade secrets may be growing. See David



As to NIH's extramural research program and the data collected on its grantees, the cost data associated with clinical trials is not legally protected information and can be disclosed by the NIH. In fact, the NIH has already disclosed this kind of detailed breakdown of costs in response to FOIA requests.<sup>219</sup> Furthermore, the federal district court in Washington, D.C. has held that grant applications to the NIH cannot be withheld from FOIA requesters on the grounds that they constitute a trade secret.<sup>220</sup> Lastly, the NIH appears to be governed by the general Health and Human Services (HHS) policies on public disclosure related to FOIA,<sup>221</sup> which indicate that the NIH retains the discretion to release information even when covered by a FOIA exemption.<sup>222</sup>

Not only does the NIH have the authority to release such information, it has stated in its grants policy that “most grant-related information submitted to NIH by the applicant or recipient in the application or in the post-award phase is considered public information”<sup>223</sup> and that “if a grant is awarded as a result of or in connection with an application, the Federal government has the right to use or disclose the information to the extent authorized by law.”<sup>224</sup>

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S. Levine, *The People's Trade Secrets?*, 18 MICH. TELECOMM. TECH. L. REV. 61 (2011). To our knowledge, the NIH has not asserted that cost information for intramural projects is protected by trade secrecy, and we agree with Professor Levine's normative assertion that there should be no governmental trade secrets.

<sup>219</sup> See *supra* note 178.

<sup>220</sup> See *Physicians Committee for Responsible Medicine v. National Institutes of Health*, 326 F. Supp. 2d 19, (D.D.C. 2004). In that case, the NIH attempted to withhold a grant application under the trade secrets exemption (5 U.S.C. § 552(b)(4) or as an inter-agency or intra-agency memorandum or letter (5 U.S.C. § 552(b)(5)). *Id.* at 20. The court held that the information was neither a trade secret nor confidential commercial information. *Id.* at 21-27. The court also rejected the notion that, as a response to a request for application (RFA), which is an “agency initiative . . . to obtain scientific expertise,” the grant application was an inter- or intra-agency memorandum. *Id.* at 27-29.

<sup>221</sup> See *Policies and Administrative Manuals that Affect the Public*, Nat'l Institutes of Health (Nov. 29, 2016), <https://www.nih.gov/institutes-nih/nih-office-director/office-communications-public-liaison/freedom-information-act-office/policies-administrative-manuals-affect-public> (providing a link to 45 CFR Part 5, the HHS rule for Freedom of Information Regulations).

<sup>222</sup> HHS states that the agency has the authority to withhold privileged and confidential information, see 45 C.F.R. § 5.31(d) (“Exemption 4 *authorizes* our agency to withhold trade secrets and commercial or financial information obtained from a person and privileged or confidential.”) (emphasis added), but does not suggest that it will uniformly withhold this information. See 45 C.F.R. § 5.42(a)(3) (“We review and consider all objections to release . . . . If we decide to release the records . . . .”).

<sup>223</sup> *NIH Grants Policy Statement 2.3.11.1*, Nat'l Institutes of Health (Dec. 2019), [https://grants.nih.gov/grants/policy/nihgps/HTML5/section\\_2/2.3.11\\_availability\\_and\\_confidentiality\\_of\\_information.htm?Highlight=trade%20secret](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_2/2.3.11_availability_and_confidentiality_of_information.htm?Highlight=trade%20secret).

<sup>224</sup> *NIH Grants Policy Statement 2.3.11.2*, Nat'l Institutes of Health (Dec. 2019), [https://grants.nih.gov/grants/policy/nihgps/HTML5/section\\_2/2.3.11\\_availability\\_and\\_confidentiality\\_of\\_information.htm?Highlight=trade%20secret](https://grants.nih.gov/grants/policy/nihgps/HTML5/section_2/2.3.11_availability_and_confidentiality_of_information.htm?Highlight=trade%20secret). In a different section, the policy lays out Freedom of Information Act procedures, stating that the NIH “generally will” release “[f]unded applications and . . . progress reports” as well as “[f]inal reports,” but “generally withhold” information related to “project personnel, such as institutional base salary information,” “[t]rade secrets,” and “[i]nformation which, if released, would



Even if the NIH is not legally barred from disclosing this information, there may be an argument that disclosure is harmful nonetheless. For example, industry has argued that sharing of R&D cost information will reveal to competitors information about a company's business strategy. As BIO stated in a memo opposing an amendment proposed by Senator Sanders to the Food and Drug Administration Safety and Innovation Act of 2012 that would impose new disclosure requirements on pharmaceutical companies, "Biopharmaceutical companies expend enormous resources on R&D and clinical development programs. However, to protect their competitive position and not tip their business strategy to competitors, private companies are not required to publicly report this information."<sup>225</sup> It is worth noting that publicly-traded pharmaceutical companies are required to report clinical trial expenditures to investors, and thus this information is already made public. KEI adds that "[i]t is true that such disclosures are in some cases more limited than those proposed by the Sanders transparency amendment, but only in degree, and not in kind, and the limitation is due to the purpose of the SEC rules on disclosures, which are to inform investors, not taxpayers or consumers."<sup>226</sup>

As applied to the NIH, we recognize that NIH grantees at universities and other research organizations may still compete for grants and awards, even though they do not compete in a market for profit. However, it is fair to require such disclosures from researchers who receive public funding. This concern is not applicable to NIH intramural research, which does not compete in the market for sale of pharmaceutical products.

In short, the NIH retains the discretion to release detailed cost information and has done so in the past. NIH's past disclosures have not harmed companies' competitive positions or universities' research, and the existence of these disclosures underscores the fact that disclosure is permissible under existing law.

## VIII. CONCLUSION

This report explains the need for cost transparency in pharmaceutical research and development and, specifically, transparency into the costs of clinical trials funded by the NIH, and proposes a set of legislative, administrative, and other reforms to achieve that goal.

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adversely affect the competitive position of the person or organization." None of these types of records should be a barrier to the information we advocate be disclosed in Section IV.

<sup>225</sup> James Love, *BIO memo opposing transparency of drug development costs, sales, prices and clinical trial outcomes*, Knowledge Economy International (May 21, 2012), <https://www.keionline.org/21844>.

<sup>226</sup> *Id.*



As discussed above, a major barrier to access to medicines, vaccines, and other medical technologies across the entire world is ever-increasing prices. Transparency into clinical trial costs, at the NIH and for all who contribute to research and development of these products, is a critical step towards lowering prices in two ways: (1) a detailed accounting of clinical trial costs will allow policymakers and the public to evaluate the pharmaceutical industry's claims that the high costs of R&D justify the extraordinarily high prices of medicines, and (2) accurate cost data will allow policymakers to design policy mechanisms that can incentivize innovation without the monopoly pricing associated with the patent system, such as grants and prizes. Though there exist a few state laws that require certain limited disclosures of R&D costs and numerous legislative proposals in Congress, there are no current requirements for cost transparency across all pharmaceutical developers, which include industry, government, academic, and philanthropic developers.

We believe all drug developers should ultimately be required to disclose costs of all aspects of R&D, but this report focuses on the costs of conducting clinical trials at the NIH. First, clinical trials are often the most expensive aspect of pharmaceutical R&D. Second, the NIH spends billions of taxpayer dollars as the largest public funder of biomedical research in the world, which in itself justifies close oversight by Congress and the public. As related to the issue of drug pricing, transparency into the costs of clinical trials run and funded by NIH would provide an important comparison to the cost estimates released by industry-funded studies, given the sheer number of clinical trials the agency conducts and funds.

This report was finalized in the midst of the COVID-19 pandemic, which has underscored the need for transparency in biomedical research and development. As the U.S. Congress allocates billions of taxpayer dollars to government research agencies and private pharmaceutical companies, the public deserves to know how that funding is spent. Furthermore, precise information on the public contribution to any drug, vaccine, or diagnostic that is developed to combat COVID-19 will be necessary to inform the inevitable pricing debates that follow the marketing of new medical technologies. Lastly, the COVID-19 pandemic has highlighted that the issues and recommendations identified here do not apply to the NIH alone, but also should be considered with respect to Biomedical Advanced Research and Development Authority (BARDA) and the Centers for Disease Control and Prevention (CDC), which have, like the NIH, already received billions of dollars in newly allocated public money to support research and development of anti-COVID vaccines, treatments, and other products.<sup>227</sup>

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<sup>227</sup> Kellie Moss et al., *The Coronavirus Aid, Relief, and Economic Security Act: Summary of Key Health Provisions*, KFF.org (Apr. 9, 2020), <https://www.kff.org/coronavirus-covid-19/issue-brief/the-coronavirus-aid-relief-and-economic-security-act-summary-of-key-health-provisions/>.



In order to offer a roadmap towards clinical trial cost transparency at the NIH, this report identifies key data points for disclosure, discusses the limited data currently disclosed by the NIH, and offers legislative, administrative, executive, and legal options for reform. Reporting clinical trial cost data disaggregated into the eight categories presented in Section IV will allow for meaningful scrutiny of those costs without being overly burdensome to report.

Given the level of detail that is necessary to accurately understand clinical trial costs, it is clear that the current level of data disclosure by the NIH is insufficient. The NIH maintains ClinicalTrials.gov (which reports clinical trial results but no cost information), RePORTER (which reports NIH grant awards), and discloses some other aggregated data online and in reports to Congress. None of these forms of data publication currently accomplishes the goal of clinical trial cost transparency, but each provides a baseline disclosure tool that can be improved to achieve greater cost transparency.

We propose that the NIH and its grantees be required to disclose disaggregated clinical trial costs on ClinicalTrials.gov. ClinicalTrials.gov is the natural home for specific clinical trial cost data because the website is already structured to collect and display detailed information about each registered trial, and only small changes would be necessary to include cost data. We propose achieving this reform by amending 42 U.S.C. § 282(j), which currently governs ClinicalTrials.gov, in two ways: (1) require that the NIH post the cost data that it possesses for any clinical trial funded in whole or in part by the NIH, and (2) require that all sponsors of clinical trials that receive NIH funding submit the cost data to the NIH to be posted on ClinicalTrials.gov upon study completion. This report also discusses other, alternative avenues for reform.

Lastly, this report addresses arguments against reform and concludes that none should stand in the way of the NIH disclosing the proposed data. We anticipate two main arguments against our proposal to require reporting of costs associated with NIH-funded clinical trials: (1) the administrative burden of additional reporting will be too high, and (2) cost information on NIH-funded clinical trials is a trade secret or confidential commercial information. We believe that cost disclosure will not be unjustifiably burdensome for three reasons. First, the NIH already requires its grantees to report disaggregated costs, which means grantees already track and the NIH already possesses disaggregated cost data on extramural research. Secondly, though we know less about how the NIH tracks its intramural research costs, it is reasonable to expect it to do so on the same level it requires of grantees. Lastly, the societal benefits of sharing cost information far outweigh potential added costs of reporting. In regard to the



purportedly confidential nature of clinical trial cost data, neither cost data on intramural research nor extramural grants have been considered trade secrets or confidential commercial information and so can legally be disclosed.

Disaggregated clinical trial cost data from the NIH is just one step towards much-needed reform to ensure fair access to medicines and other medical technologies. There are no legal barriers to disclosure of clinical trial costs, and the existing NIH-run ClinicalTrials.gov database provides a built-in structure to implement this proposal.

## **IX. ABOUT THE CLINIC, ACKNOWLEDGMENTS, AND COPYRIGHT NOTICE**

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*Acknowledgments:*

The authors and editor gratefully acknowledge and thank the following individuals for their very helpful input, which included encouragement, guidance, factual research, correction, and criticism at various points during the research and writing process: Luis Gil Abinader, Ava Alkon, Kathryn Ardizzone, Anna Birkenbach, Claire Cassidy, Rachel Cohen, Dana Gill, Victoria Gimenez, Dzintars Gotham, Susan Hodges, Gaëlle Krikorian, Jamie Love, Peter Lurie, Manuel Martin, Elisabeth Massute, Suerie Moon, Jason Nickerson, Jason Schultz, Roz Scourse, Temmy Sunyoto, Adrian Towse, Marcela Vieira, Laurence Vielfaure, Michael Weinberg, Olivier J. Wouters, and Deborah Zarin. The views expressed in this white paper do not necessarily reflect the views of these acknowledged individuals.

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