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Response to "Department of Commerce, National Institute of Standards and Technology, Agency Information Collection Activities"

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DEPARTMENT OF COMMERCE
National Institute of Standards and Technology
Agency Information Collection Activities
Submission to: Office of Management and Budget (OMB) for Review and Approval
Comment Request: iEdison System

Agency: National Institute of Standards and Technology (NIST), Commerce.

Action: Notice of information collection, request for comment.

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This response **supports the recommendations of the interagency working group** for Bayh-Dole that the dataset collected and archived in iEdison "*…be amended and expanded so that the agencies could get a clear picture of the commercialization plans for subject inventions, what the licensing landscape looked like, (and) what products were resulting, …*"

Our comments are informed by several recent studies[1] describing the effectiveness and reach of the Bayh-Dole Act in promoting and protecting the public interest in practical applications of government-funded biomedical research to pharmaceutical innovations. Specifically, we make three recommendations based on these studies:

1. **Additional information is required on the nature and number of "subject invention" disclosures arising from government-funded research and the reasons for attrition through patent filing, prosecution, and issuance.**

2. **Additional information is required on the terms of license agreements between the Contractor and the commercialization partner that provide the public sector with a return on government investments**.

3. **Additional data is required on government investments in basic science, as well as applied research to meaningfully assess the return on investment.**

[1] Portions of these comments are extracted from Cleary, EG, Jackson MJ, Zhou EW, Ledley FD. (2023) Comparison of Research Spending on New Drug Approvals by the National Institutes of Health vs the Pharmaceutical Industry, 2010-2019. JAMA Health Forum. 2023;4(4):e230511; Ledley and Cleary (2023) NIH funding for patents that contribute to market exclusivity of drugs approved 2010–2019 and the public interest protections of Bayh-Dole. PLOS ONE https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0288447; Shah, P., Vaughan G., Ledley, F.D. (2023) Comparing the economic terms of biotechnology licenses from academic institutions with those between commercial firms. PLOS ONE journals.plos.org/plosone/article?id=10.1371/journal.pone.0283887

Background

Our comments focus on the statement in the notice that iEdison is intended to "*provide data for calculation of return on investment (ROI) from federal funding*." We agree this should be a priority. We also believe that this understates the fact that Bayh Dole represents the only significant statutory instrument for promoting and protecting the public's interest in the practical benefits derived from government funded research, the direct economic returns associated with licensing government-funded inventions for commercialization, and the indirect returns of innovation on jobs and economic growth.

The stated objectives of the Bayh-Dole Act are to "*…promote the utilization of inventions arising from federally supported research or development…*," advance "*…the commercialization and public availability of inventions made in the United States by United States industry and labor…*," and protect the public "*…against nonuse or unreasonable use of inventions"*.[2] By promoting commercialization of practical applications enabled by federally funded research, Bayh-Dole was designed to provide returns to the public sector in the form of commercial products to address unmet public needs, create jobs, stimulate economic growth, and expand the tax base.[3] Additionally, by ceding the revenues from technology licenses to non-profit institutions incorporated in the public interest,[4] Bayh-Dole positioned these institutions as proxies for the public sector in securing a direct return on public investment. To this end, Bayh-Dole further authorized these institutions to retain the proceeds from such licenses, providing that the proceeds are shared with the inventor and that institutional funds "*will be utilized for the support of scientific research or education*."[5]

Recent economic studies contextualize government's contributions to innovation as that of an "*early-stage investor*" and government funding for research as an "*investment.*" As such, these studies argue there should be an equitable balance of investment risk and return between the public and private sectors and frame the role of policy as shaping this balance[6] in which the public and private sector both receive returns on investment commensurate with the risk of these investments. If iEdison is to achieve the goal of "providing data for calculation of return on investment from federal funding" it must be expanded to encompass the multivariate forms of value generated by these investments.

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[2] CFR. Code of Federal Regulations, Title 37 Part 401 RIGHTS TO INVENTIONS MADE BY NONPROFIT ORGANIZATIONS AND SMALL BUSINESS FIRMS UNDER GOVERNMENT GRANTS, CONTRACTS, AND COOPERATIVE AGREEMENTS Code of Federal Regulations 2010 [cited 2020 July 3, 2020]. Available from: https://www.govinfo.gov/content/pkg/CFR-2010-title37-vol1/pdf/CFR-2010-title37-vol1-part401.pdf.

[3] Sampat BN. Patenting and US academic research in the 20th century: The world before and after Bayh-Dole. Research Policy. 2006;35(6): p. 772–789; Federal Council for Science and Technology, Effects of Government Policy on Commercial Utilization and Business Competition, Government Patent Policy Study, final report. Federal Council for Science and Technology, 1968; Bray MJ, Lee JN. University revenues from technology transfer: Licensing fees vs. equity positions. J Bus Ventur. 2000;15(5-6): p. 385–392.

[4] Salamon LM. The new governance and the tools of public action: An introduction. Fordham Urb. LJ. 2000;28: p. 1611.

[5] Ouellette LL, Weires R. University Patenting: Is Private Law Serving Public Values? Michigan State Law Review. 2020;2019(5): p. 1328-1387.

[6] Mazzucato M, Li H. The entrepreneurial state: socializing both risks and rewards. Real-World Economics Review. 2018;84; Mazzucato M. An entrepreneurial society needs an entrepreneurial state. Harv Bus Rev. 2016:1-4; Lazonick W, Mazzucato M. The risk-reward nexus in the innovation-inequality relationship: who takes the risks? who gets the rewards? Industrial and Corporate Change. 2013;1093-1128; Laplane A, Mazzucato M. Socializing the risks and rewards of public investments: economic, policy, and legal issues. Research Policy. 2020;49: ; Cleary EG, Jackson MJ, Zhou EW, Ledley FD. (2023) Comparison of research spending on new drug approvals by the US National Institutes of Health versus industry, 2010-2019. JAMA Health Forum https://jamanetwork.com/journals/jama-health-forum/fullarticle/2804378; Cleary EG, Jackson MJ, Ledley FD (2020) Government as the first investor in biopharmaceutical innovation; evidence from new drug approvals 2010–2019. (revised 2021) Institute for New Economic Thinking. www.ineteconomics.org/uploads/papers/WP_133-Revised-2021.0719-Cleary-Jackson-Ledley.pdf

Based on our research, we offer three specific recommendations:

1. Additional information is required on the nature and number of "subject invention" disclosures arising from government-funded research and the reasons for attrition through patent filing, prosecution, and issuance.

Table 1[7] shows the NIH funding for basic or applied research associated with 313 drugs approved 2010-2019 with entries in DrugPatentWatch. The study identified publications in PubMed (PMID) related to the drug target (basic research) or the drugs (applied research), estimated the number of years of project funding related to that research (project years) and costs for those project years.[8] The study identified $164 billion in NIH funded resarch involving >341 thousand project years of NIH funding contributing to these products, while the patents associated with these drugs in DrugPatentWatch represented research totaling only $954 million and only 769 project years of government funded research.

Table 1. HIN funding for research leading to patents in DrugPatentWatch associated with drugs approved 2010–2019.

	Total[1]	Applied research (% total)	Basic research (% total)
NIH-funded research on drugs approved 2010–2019 listed in DrugPatentWatch (n=313)			
Searches	n/a	313	194
PMIDs	349,797	33,048 (9%)	316,749 (91%)
Project Years[2]	341,375	45,200 (13%)	296,175 (87%)
Project Year Costs (project funding years only, millions)	$163,878	$28,553 (17%)	$135,325 (83%)
NIH-funded research related to DrugPatentWatch patents associated with drugs approved 2010–2019			
Patents	104	61 (59%)	43 (41%)
PMIDs	4,030	546 (14%)	3,484 (86%)
Project Years[2]	769	242 (31%)	527 (69%)
Project Year Costs (project funding years only, millions)	$954.0	$436.7 (46%)	$517.3 (54%)

[1] Includes both applied and basic research. [2] NIH RePORT data 2000-2019.

Table 2 shows that there were 6,344 patents in DrugPatentWatch associated with the 313 drugs approved 2010-2019. There were 22,409 patents identified with the NIH-funded projects that contributed to basic or applied research related to thee products.[9] Of these, only 104 of the patents in DrugPatentWatch were associated with NIH-funded resarch related to these drugs or their targets. Moreover, while NIH-funded research was associated with all of the 313 drugs in this study, only 29 (9.3%) had patents arising from this NIH-funded research.

Table 2. Number of new drug approvals 2010–2019 associated with NIH-funded patents.

	# drugs
Drugs approved 2010-2019 with entry in FDA Orange Book or DrugPatentWatch[1]	313
…with at least one patent in FDA Orange Book or DrugPatentWatch	297
	# patents
…associated patents in FDA Orange Book or DrugPatentWatch	3,644
	Cleary dataset[2]
NIH-funded patents related to drugs approved 2010–2019	22,409
…number in FDA Orange Book or DrugPatentWatch (% associated patents)[3]	104 (2.9%)
	# drugs
Drugs with NIH-funded FDA Orange Book or DrugPatentWatch patents (% drugs)[4]	29 (9.3%)

[1] DrugPatentWatch includes all active and expired patents from the FDA Orange Book and certain additional patents on biological products identified by companies or patent search. [2] Cleary identified NIH-funded projects associated with drugs approved 2010–2019 or their targets as well as patents arising from these projects [2]. [3] Percentage of patents in FDA Orange Book or DrugPatentWatch associated with drugs approved 2010–2019. [4] Percentage of drugs approved 2010–2019 listed in FDA Orange Book or DrugPatentWatch. n/a – not applicable.

[7] From Ledley and Cleary (2023) *op cit*. Tables and portions of the text have been extracted from that publication.

[8] The method is described in detail and available as a dashboard at

[9] Note: The RePORTER database does not allow association of patents with specific project years of research funding. Thus, the 22,409 patents include research funded by the same project that contributed to basic or applied research on these drugs, but not necessary the publications directly related to these drugs or their targets. See Ledley and Cleary (2013) *op cit* for details.

Overall, only 0.56% of NIH funding for research directly related to the drugs approved by the FDA from 2010-2019 was represented in patents cited in DrugPatentWatch,[10] including only 0.38% of NIH funding for basic research on drug targets and 1.5% of NIH funding for applied research on the drugs themselves.

It is recognized that a mature body of basic biomedical research is requisite for drug approvals[11] Basic research is defined as "*…experimental or theoretical work undertaken primarily to acquire new knowledge of the underlying foundations of phenomena and observable facts, without any particular application or use in view,*"[12] though it may be "*use inspired*."[13] Without a focus on particular applications, basic research is less likely to satisfy USPTO standards for a patentable invention, which require demonstration of utility and enablement in addition to novelty.[14] It is currently unknown how many disclosures are filed by Contractors pursuant to Bayh Dole and the fate of those disclosures.

Specific recommendation

Basic research that does not lead to disclosure of a subject invention does not trigger Bayh Dole or reporting to iEdison. It is likely however, that universities receive disclosures of basic research findings and choose not to move forward with a patent filing based on their assessment of utility and enablement provided by the disclosure. Similarly, many patent applications are rejected by the USPTO based on inadequate demonstrations of utility or enablement. **Additional information should be collected on reasons that universities choose not to pursue a provisional or full patent filing on subject inventions as well as the reasons that a patent application may be abandoned or rejected by the USPTO.** While this would not systematically capture all basic research, it would provide a more complete picture of the scope of the government contribution to innovation.

This can be done without undue reporting burden using a checklist of reasons that the technology transfer office or USPTO cite for rejection (i.e. lack of novelty, utility, or enablement). While beyond the scope of our comments, we would also note that with recent advances in AI, archiving of critical text including patent applications, communications with examiners, or internal reports may be of far greater value than checklists of selected information and may further reduce the regulatory burden.

2. Additional information is required on the terms of license agreements between the Contractor and the commercialization partner that provide the public sector with a return on government investments.

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[10] DrugPatentWatch is a registered trademark of thinkBiotech LLC available at www.drugpatentwatch.com. The dataset incorporates patents cited in the FDA Orange Book or cited in litigation.

[11] McNamee LM, Ledley FD. (2017) Modeling timelines for translational science in cancer; the impact of technological maturity. PLOS ONE 12.3, e0174538, journals.plos.org/plosone/article?id=10.1371/journal.pone.0174538; McNamee LM, Walsh MJ, Ledley FD. (2017) Timelines of translational science: From technology initiation to FDA approval. PLOS ONE. 12.5 e0177371; Beierlein JM, McNamee LM, Walsh MJ, Kaitin KI, DiMasi JA, Ledley FD. (2017) Landscape of innovation for cardiovascular pharmaceuticals: from basic science to new molecular entities. Clinical Therapeutics. 39: 1409-1425 e20

[12] NSF. Definitions of Research and Development: An Annotated Compilation of Official Sources. 2018.

[13] Stokes DE. Pasteur's quadrant: Basic science and technological innovation. Brookings Institution Press; 2011.

[14] USPTO. Manual of Patent Examining Procedure. Requirements for Specification Under 35 U.S.C. 112, First Paragraph 2020. https://mpep.uspto.gov/RDMS/MPEP/e8r9#/result/d0e213359.html?q=enablement&ccb=on&ncb=off&icb=off&fcb=off&ver=e8r9&syn=adj&results=compact&sort=relevance&cnt=10&index=1.

Figure 1[15] shows the economic returns from academic licenses to commercial firms as well as those between ccommercial entities derived from BioSciDB[16] including the effective royalty rate on $500M in net sales, total reported deal size; and total precommercial payments. There were statistically significant differences between the returns to academic institutions from biotechnology licenses and those of licenses between commercial entities. Academic licenses had lower effective royalty rates (median 3% versus 8%, p<0.001), deal size (median $0.9M versus $31.0M, p<0.001), and precommercial payments (median $1.1M versus $25.4M, p<0.001) than corporate licenses. Controlling for the clinical phase of the most advanced product included in the license reduced the median difference in effective royalty rate between academic and corporate licenses from 5% (95% CI 4.3–5.7) to 3% (95% C.I. 2.4–3.6) but did not change the difference in deal size or precommercial payments. Excluding licenses for co-commercialization did not change the effective royalty rate but reduced the median difference in deal size from $15.8M (95% CI 14.9–16.6) to $11.4M (95% CI 10.4–12.3) and precommercial payments from $9.0M (95% CI 8.0–10.0) to $7.6M (95% CI 6.8–8.4). Controlling for deal terms including exclusivity, equity, or R&D in multivariable regression had no substantive effect on the difference in economic terms.

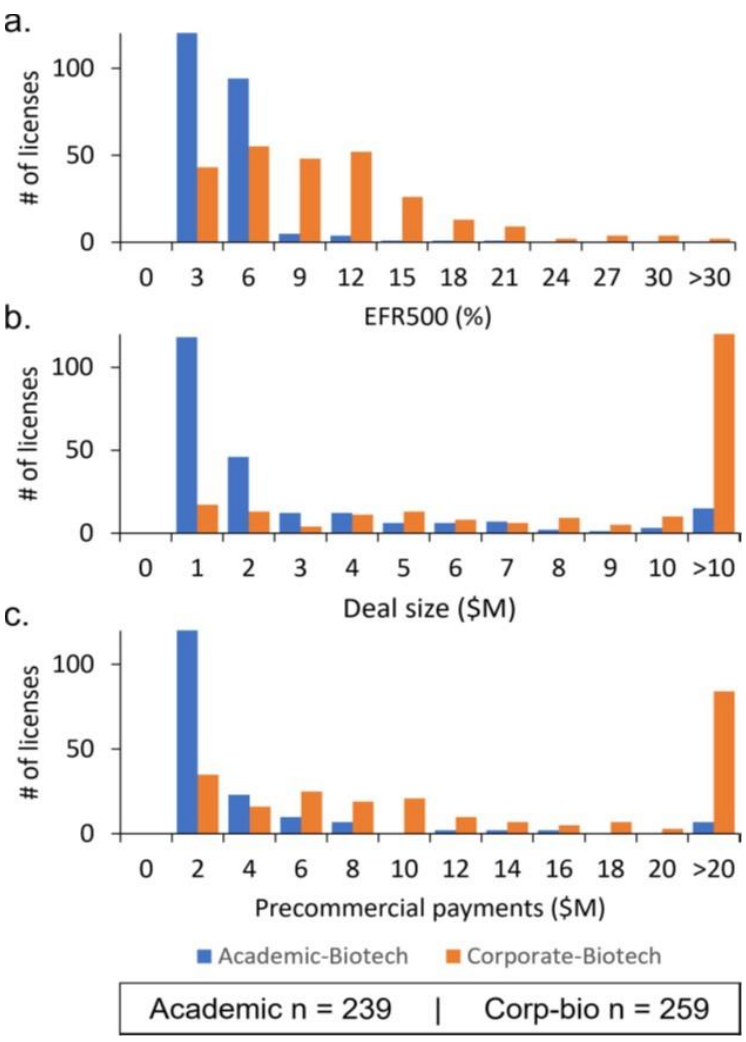

Figure 1. From Shat et al (2023) op cit

This research demonstrated that the economic returns to academic institutions from licenses of biotechnologies arising from federally funded research are substantially lower than those of comparable licenses between commercial firms. While the absolute value of the economic returns is influenced by the development stage of products, whether the licensee was a biotechnology or large pharmaceutical company, and whether the license agreement involved co-commercialization, the disparity between academic and corporate licenses is largely independent of these factors. There is currently no data

[15] From Shah et al.,(2023) *op cit*. Tables and portions of the text have been extracted from that publication.
[16] The BioScience database (now BioSciDB, part of Evaluate Ltd.) was provided courtesy of Mark Edwards.

resource available to systematically assess the returns to licenses granted pursuant to Bayh Dole[17] and whether these returns satisfy the legal standard of a "reasonable royalty rate."[18]

Specific recommendation

Additional information should be collected on the terms of license agreements between Contractors and their commercialization partners. This data should include the financial terms (i.e. royalty rate, precommercial payments, milestones, etc.), the development stage of products anticipated through the alliance (basic research, applied preclinical research, phase 1, phase 2, phase 2, NDA/BLA, approved) as well as key terms of the agreement related to co-commercialization. exclusivity, field, R&D payments, patent prosecution, and future options and responsibilities under the agreement.

This can be done without undue reporting burden using a checklist of common license terms. As noted above, with recent advances in AI, archiving of the license agreements themselves may be of far greater value than questionnaires asking for selected information and may further reduce the regulatory burden.

3. Additional data is required on government investments in basic science, as well as applied research to meaningfully assess the return on investment.

It is generally recognized that government plays a central role in funding the basic science that underlies innovation. As noted above, government funded basic research is not primarily concerned with a specific application in mind and is, thus, less likely to generate a "subject invention."[19] Since the provisions of Bayh Dole are only triggered by disclosure of a subject invention, these early government investments that are lead to innovation are not necessarily represented in iEdison.

[17] Data in the BioScience database contains licenses agreements reported to the SEC obtained through FOIA petitions. The dataset is thus limited to licensed that a company considers "material" to their valuation. "Materiality" is legally defined as *"a substantial likelihood that the disclosure of the omitted fact would have been viewed by the reasonable investor as having significantly altered the 'total mix' of information*" and is assessed in relation to the significance of an item to users of a registrant's financial statements" (SEC, 1999). See: FASB, Amendments to Statement of Financial Accounting Concepts No. 8. Conceptual Framework for Financial Reporting Chapter 3, Qualitative Characteristics of Useful Financial Information. 2018, Financial Accounting Standards Board; Securities and Exchange Commission (SEC), SEC Staff Accounting Bulletin: No. 99–Materiality, August 1999; SCOTUS, MATRIXX INITIATIVES, INC., ET AL. v. SIRACUSANO ET AL. CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT No. 09–1156. SCOTUS 2011.

[18] A "reasonable royalty rate" is defined as "t*he amount which a prudent licensee who desired, as a business proposition, to obtain a license to manufacture and sell a particular article embodying the patented invention would have been willing to pay as a royalty and yet be able to make a reasonable profit and which amount would have been acceptable by a prudent patentee who was willing to grant a license.*" See Ouellette LL, Weires R. University Patenting: Is Private Law Serving Public Values? Michigan State Law Review. 2020;2019(5): p. 1328-1387; Jarosz JC, Chapman MJ. The Hypothetical Negotiation and Reasonable Royalty Damages: The Tail Wagging the Dog. Stan. Tech. L. Rev. 2012;16: p. 769; Seaman CB. Reconsidering the Georgia-Pacific standard for reasonable royalty patent damages. BYU L. Rev. 2010: p. 1661.

[19] The Bayh-Dole Act defines a subject invention as "*…any invention of a contractor conceived or first actually reduced to practice in the performance of work under a funding agreement" and further requires that it must be "conceived or first actually reduced to practice in performance of the project.*" See: 27.Title 35 U.S. Code Chapter 18—Patent rights in inventions made with federal assistance, as amended Nov 1, 2000 (1980).

Table 3 shows the NIH-funded publications, project years of NIH funding, and costs associated with basic or applied research on the 356 drugs approved 2010-2019.[20] These data show that approximately 83% of the government funded research related to these products represented basic research on the drug targets, rather than applied research on the drugs themselves. Thus, a significant fraction of the government investment in innovation may not trigger disclosures under Bayh Dole and may not be represented in iEdison.

Table 3. NIH funding for basic and applied research related to 356 NMEs approved by the FDA, 2010–2019

	DRUG Search[a]	TARGET Search[b]	Total
PubMed search results			
# Searches	356	217	
# Publications in PubMed (1985-2019)	229,401	1,911,507	2,017,408[c]
RePORT NIH-funded publications			
# Publications with NIH funding (1985-2019)	36,195	409,123	424,293[c]
% Publications with NIH funding	16%	21.4%	21%
Totals			
# Searches identifying publications with NIH funding	310	217	
% Searches identifying publications with NIH funding	87%	-100%	
RePORT Project Years and Costs	**Applied Research[d]**	**Basic Research[d]**	**Total**
# Project Years	42,549	317,354	359,903
Project Years costs ($ millions)	$30,954	$156,429	$187,383
% Total NIH funding	17%	83%	

[a]PubMed search performed with drug name and synonyms. [b]PubMed search performed with name of biological target. [c]Total is nonadditive due to publications identified in both drug and target searches. [d]Publications identified in a drug search are classified as applied research. Publications identified in a target search, but not a drug search, are classified as basic research.

Any calculation of the return on government investments requires an accurate measure of the cost basis of that investment. Estimates of NIH funding based solely on government contributions to development research (i.e. phased clinical trials) [21] or patents[22] fail to capture the major contribution made by government investment in basic science and any calculation of the return on investment based on these estimates of the cost basis are inherently flawed.

Specific recommendation

New approaches to assessing the full scope of government investment in both basic and applied research (including development) need to be developed to fairly assess the return on these

[20] Cleary E et al (2023) *op cit*; see also working paper Cleary et al., (2020) Institute for New Economic Thinking, *op cit*.
[21] See: Zhou et al (2023) *op cit*; Nayak RK, Lee CC, Avorn J, Kesselheim AS. Public-sector Contributions to Novel Biologic Drugs. JAMA Intern Med. 2021;181(11):1522-1525; Abinader LG. Role of Private Sector, Governments and Charities in Funding Research and Development Related to Tocilizumab. KEI Research Note 2020:2. https://www.keionline.org/wp-content/uploads/KEI_Research_Note_2020_2_Government_Funding_IP_Tocilizumab.pdf; Ardizzone K. Role of the Federal Government in the Development of Remdesivir. KEI Briefing Note 2020:1. https://www.keionline.org/wp-content/uploads/KEI-Briefing-Note-2020_1GS-5734-Remdesivir.pdf; Unger JM, Nghiem VT, Hershman DL, Vaidya R, LeBlanc M, Blanke CD. Association of National Cancer Institute–Sponsored Clinical Trial Network Group Studies With Guideline Care and New Drug Indications. JAMA Network Open. 2019;2(9):e1910593-e1910593.
[22] Ledley and Cleary (2023) *op cit*; Azoulay P, Graff Zivin JS, Li D, Sampat BN. Public R&D investments and private-sector patenting: evidence from NIH funding rules. The Review of economic studies. 2019;86(1):117; Li D, Azoulay P, Sampat BN. The applied value of public investments in biomedical research. Science. 2017;356(6333): 78–81.

investments. The methods described by Cleary et al[23] for identifying government investments in both basic and applied science related to new drugs are not generalizable to innovation in other sectors. As noted above, some fraction of government-funded basic research may be represented in disclosures by faculty that do not result in patent filings are declined because, in the judgement of the technology transfer office, the findings to not meet the standards for an invention. A rigorous assessment of the return on government investments in research will require development of new methodologies for connecting basic research to the practical applications enabled by this research. We call on NIST to solicit expert opinion and fund research aimed at enabling such an assessment.

Conclusion

In closing, we applaud the initiative by NIST to broaden the scope of the data collected and archived in iEdison for the purposes listed. We hope this initiative is successful and iEdison becomes a more powerful tool for not only assessing the effectiveness of government investment in American innovation, but continuously improving the process by which government funded research provides the public with practical applications that improve their wellbeing and an equitable return on investment.

Fred D. Ledley, M.D.
July 3, 2023

[23] Cleary et al. (2020) *op cit*; Cleary et al (2023) *op cit*; Cleary EG, Beierlein JM, Khanukja N, McNamee LM, Ledley FD. (2018) Contribution of NIH funding to new drug approvals 2010-2016. Proceedings of the National Academies of Science. 115(10), pp.2329-2334.