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Comments Re: Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer

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Written comments re:	**Workshop on Transforming Discoveries into Products: Maximizing NIH's Levers to Catalyze Technology Transfer**
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We are pleased to offer written comments to this workshop focused on "*… making federally funded inventions more accessible to the public…* ." These comments are informed by recent research from the Center for Integration of Science and Industry at Bentley University that has:

- Quantified the scope of NIH funding for basic or applied research, clinical development, or patents associated with drugs approved by the FDA 2010-2019. [2] This work identified $187 billion in NIH-funded research directly related to these drugs (applied research – 17%) or their biological targets (basic research – 83%),[3] representing a (discounted) investment comparable to reported levels of investment by industry, thus reducing the investment required by industry by approximately half.[4] These studies further show that less than 3.5% of this funding contributing to phased clinical trials[5] and <1% resulted in patents cited as providing market exclusivity and subject to the public interest protections of Bayh-Dole.[6]
- Compared the financial returns of biotechnology license from academic institutions with those between commercial firms.[7] This work demonstrated that the effective royalty rates and other payments associated with licenses of academic technologies under Bayh-Dole were less than half of those between commercial firms independent of the development stage of products anticipated under these Agreements or other intrinsic terms of the Agreements.
- A novel approach to quantify the "health value" or direct health benefit realized by individuals taking specific pharmaceutical products independent of impacts on economic activity or indirect, econometric inferences.[8]

Specifically, we would like to offer four comments:

1. The NIH makes investments in new drug approvals comparable to those of industry. While the NIH contributes primarily to early-stage, basic research, rather than applied research or development, evidence shows that this established foundation of basic science is requisite for successful product development. As such**, the public sector should expect normative returns on NIH investments in new drugs comparable to those of the biopharmaceutical industry.**
2. The restriction of the Bayh-Dole Act to "subject inventions" limits the Act's applicability to the results of basic research. **Effort should be directed at demonstrating the utility and enablement**

[2] Cleary, EG, Beierlein, JM, Khanuja, NS, McNamee, LM, & Ledley, FD (2018). Contribution of NIH funding to new drug approvals 2010–2016. Proceedings of the National Academy of Sciences, 115(10), 2329-2334. https://www.pnas.org/doi/abs/10.1073/pnas.1715368115; 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, https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0288447; Zhou, Edward W., Matthew J. Jackson, and Fred D. Ledley. "Spending on Phased Clinical Development of Approved Drugs by the US National Institutes of Health Compared With Industry." *JAMA Health Forum*. Vol. 4. No. 7. American Medical Association, 2023. https://jamanetwork.com/journals/jama-health-forum/fullarticle/2807184; 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; Cleary, E.G., Jackson, M.J., Ledley, F.D. (2020) Government as the First Investor in Biopharmaceutical Innovation: Evidence From New Drug Approvals 2010–2019 Institute for New Economic Thinking, Working Paper No. 133, August 5th, 2020 (Revised July 19th , 2021) https://www.ineteconomics.org/uploads/papers/WP_133-Revised-2021.0719-Cleary-Jackson-Ledley.pdf

[3] Cleary et al., (2018) op cit; Cleary et al (2020) op cit; Cleary et al (2023), op cit.

[4] Cleary et al. (2023) op cit

[5] Zhou et al., (2023) op cit

[6] Ledley and Cleary (2023) op cit

[7] 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;

[8] Chaves da Silva, P. and Ledley, FD unpublished data

provided by NIH-funded basic science to ensure that the public interest provisions of the Act apply to a larger fraction of NIH-funded research.

3. Licenses of biotechnologies originating in academic institutions embody financial terms that are significantly less favorable than those of comparable licenses between commercial firms. **Additional effort needs to be made to establish that a "reasonable royalty rate" for academic licenses requires financial terms comparable to those of corporate licenses.**
4. **Impact indicators should be developed that measure the direct, measurable impacts of innovative pharmaceuticals on individuals and their health rather than indirect impacts on economic indicators or broad measures of population health.**

Background

The Bayh-Dole Act represents the only significant statutory instrument for promoting and protecting the public's interest in the health benefits arising from government-funded biomedical research and the products enabled by this research, direct economic returns from commercialization of these products, and indirect returns impacts on jobs, productivity, and economic growth. This is evident in the stated objectives of the Bayh-Dole Act 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"*.[9]

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.[10] Additionally, by ceding the revenues from technology licenses to non-profit institutions incorporated in the public interest,[11] 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*."[12]

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[13] in which the public and private sectors both receive returns on investment commensurate with the risk of these investments.

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[9] 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.

[10] 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.

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

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

[13] 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.

Based on our research, we offer three specific suggestions:

1. The public sector should expect normative returns on NIH investments in new drugs comparable to those of the biopharmaceutical industry.

Figure 1 shows a schematic of NIH funding for basic or applied research prior to first approval of drugs approved from 2010-2019.[14] NIH data includes NIH-funded projects related to: (i) the drug target (basic research) after accounting for spillover effects in which research on each drug target is associated with 2.85 approved products[15] (ii) the drug product (applied research) including phased clinical trials. Industry costs include the costs of phased clinical trials and "pre-human" studies. Statistical analysis demonstrates that the NIH spending on each new drug prior to first approval was not less than reported industry costs using different scenarios.[16] We call on the NIH to promote policies based on the expectation that the return on public investments in pharmaceutical innovation should not be less than the returns on private investment.

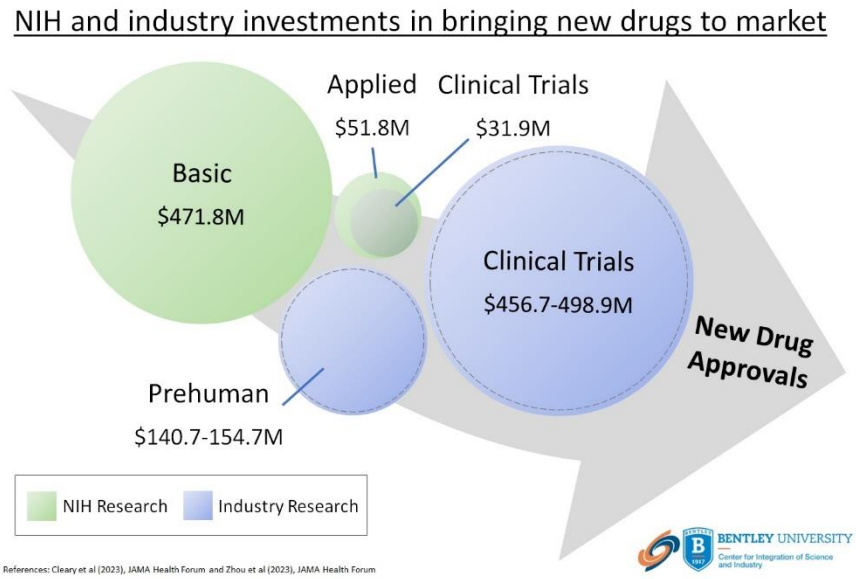

Figure 1. Average contributions of NIH and industry to first approval of novel pharmaceuticals 2010-2019. Data is based on NIH funding for basic research on drug targets, applied research on the drug (including clinical trials), and reported investments by industry from DiMasi et al (2016) or Wouters (2020).

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, et al (2023) op cit; Cleary EG, et al (2020) op cit G

[14] NIH data from Cleary et al., (2023) op cit; Zhou et al., (2023) op cit. Industry data from DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. Journal of health economics. 2016 May 1;47:20-33. https://www.sciencedirect.com/science/article/abs/pii/S0167629616000291; Wouters OJ, McKee M, Luyten J. Estimated research and development investment needed to bring a new medicine to market, 2009-2018. Jama. 2020 Mar 3;323(9):844-53. https://jamanetwork.com/journals/jama/article-abstract/2762311

[15] The number of drug approvals/target was estimated from Santos R, Ursu O, Gaulton A, Bento AP, Donadi RS, Bologa CG, Karlsson A, Al-Lazikani B, Hersey A, Oprea TI, Overington JP. A comprehensive map of molecular drug targets. Nature reviews Drug discovery. 2017 Jan;16(1):19-34. https://www.nature.com/articles/nrd.2016.230%E2%80%B3

[16] Cleary et al. (2023) op cit.

2. Effort should be directed at demonstrating the utility and enablement provided by NIH-funded basic science to ensure that the public interest provisions of the Act apply to a larger fraction of NIH-funded research.

It is generally recognized that government plays a central role in funding the basic science that underlies innovation. 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,*"[17] though it may be "*use inspired.*"[18]

Table 1 shows the NIH-funded publications, project years of NIH funding, and costs associated with basic or applied research for drugs approved by the FDA from 2010-2019.[19] The method involves identifying publications in PubMed (PMID) related to the drug target (basic research) or the drugs (applied research), estimates the number of years of project funding related to that research (project years) and costs for those project years.[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.

Table 1. NIH funding for basic and applied research related to 356 NMEs approved by the FDA, 2010-

	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.

While there is evidence that an established body of basic biomedical research on drug targets or technological components of a product is requisite for drug approval[21] basic research is not primarily

[17] NSF. Definitions of Research and Development: An Annotated Compilation of Official Sources. 2018.
[18] Stokes DE. Pasteur's quadrant: Basic science and technological innovation. Brookings Institution Press; 2011.
[19] Cleary E et al (2023) *op cit*; see also working paper Cleary et al., (2020) Institute for New Economic Thinking, *op cit*.
[20] The method is described in detail and available as a dashboard for public use at https://www.bentley.edu/centers/center-integration-science-and-industry/nih-funding-drug-innovation-dashboard

[21] 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

concerned with applications and, thus, less like to generate a "subject invention"[22] than applied research and less likely to satisfy USPTO standards for patentability, which requires demonstration of utility and enablement in addition to novelty.[23]

This dynamic may be responsible for the observation that <1% of this NIH funding was represented in patents cited in DrugPatentWatch[24] (which includes the FDA Orange Book) and that these patents arose disproportionately from applied, rather than basic, research.[25] Our research identified NIH funding for basic or applied research related to each of the 313 drugs approved 2010-2019 with entries in DrugPatentWatch.[26] Table 2 shows that there were 6,344 patents in DrugPatentWatch associated with drugs approved 2010-2019. There were 22,409 patents identified as arising from NIH-funded projects that produced basic or applied research related to these products in RePORTER.[27] Only 104 of these

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.

patents were cited in DrugPatentWatch in association with these products. Moreover, while NIH-funded research was associated with each of the 313 drugs approved 2010-2019 with citations in

[22] 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).

[23] 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

[24] 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 regarding market exclusivity.

[25] Ledley and Cleary (2023) op cit

[26] This dataset for this project was somewhat smaller than the 356 drug approvals from 2010-2019 and $187 billion in NIH funding described in Cleary et al (2020) and Cleary et al (2023) due to the fact that not all approved products are covered by the Hatch-Waxman Act and included in the FDA Orange Book. While the DrugPatentWatch database expands on Orange Book dataset to include certain biological product, the current project restricted the dataset to the 313 products with at least one patent cited in this database.

[27] 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.

DrugPatentWatch, only 29 (9.3%) had patents arising from this NIH-funded research. 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, 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.

There is little publicly available data on the fraction of NIH-funded projects that produce disclosure of possible subject inventions or the fraction of such disclosures that lead to patent filing or licenses.[28] It is, thus, unclear whether the basic science research that enables drug approvals is not reported as a possible subject invention, is not pursued by technology transfer offices, or leads to patent applications that are rejected by the USPTO for inadequate demonstration of utility or enablement. In any case, the result is that little of the NIH-funded research that enables new drug approvals is subject to the public interest protections of Bayh-Dole designed to promote commercialization of products that represent practical applications of this research and the reasonable availability of these products to the public.

While the patent-centric design of the Bayh-Dole Act is beyond the scope of this research, we call on the NIH to support research on an experimental and theoretical basis for establishing that NIH-funded basic science, in fact, enables new drug discovery and development sufficient to satisfy the definition of a "subject invention" as well as USPTO standards of "utility," and "enablement." Information should also be collected and made public concerning the scope of disclosures under Bayh-Dole, the reasons universities or the NIH may 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. Only by working to make NIH-funded basic research subject to the public interest provisions of Bayh-Dole can the technology transfer process operationalized by the Act ensure that the public interest in the fruits of this research is protected and the public receives an equitable return on their investment in pharmaceutical innovation.

3. Additional effort needs to be made to establish that a "reasonable royalty rate" for academic licenses requires financial terms comparable to those of corporate licenses.

Figure 2[29] shows the economic returns from academic licenses to commercial firms as well as those between commercial entities derived from BioSciDB[30] 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

[28] While there is mandatory reporting of these events under Bayh-Dole, the Act also prohibits public disclosure of this information See: Rai AK, Sampat BN. Accountability in patenting of federally funded research. Nature biotechnology. 2012 Oct;30(10):953-6. https://www.nature.com/articles/nbt.2382

[29] From Shah et al.,(2023) *op cit*. Tables and portions of the text have been extracted from that publication.

[30] The BioScience database (now BioSciDB, part of Evaluate Ltd.) was provided courtesy of Mark Edwards.

$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.

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 resource available to systematically assess the returns to licenses granted pursuant to Bayh Dole[31] and whether or not these returns satisfy the legal standard of a "reasonable royalty rate."[32]

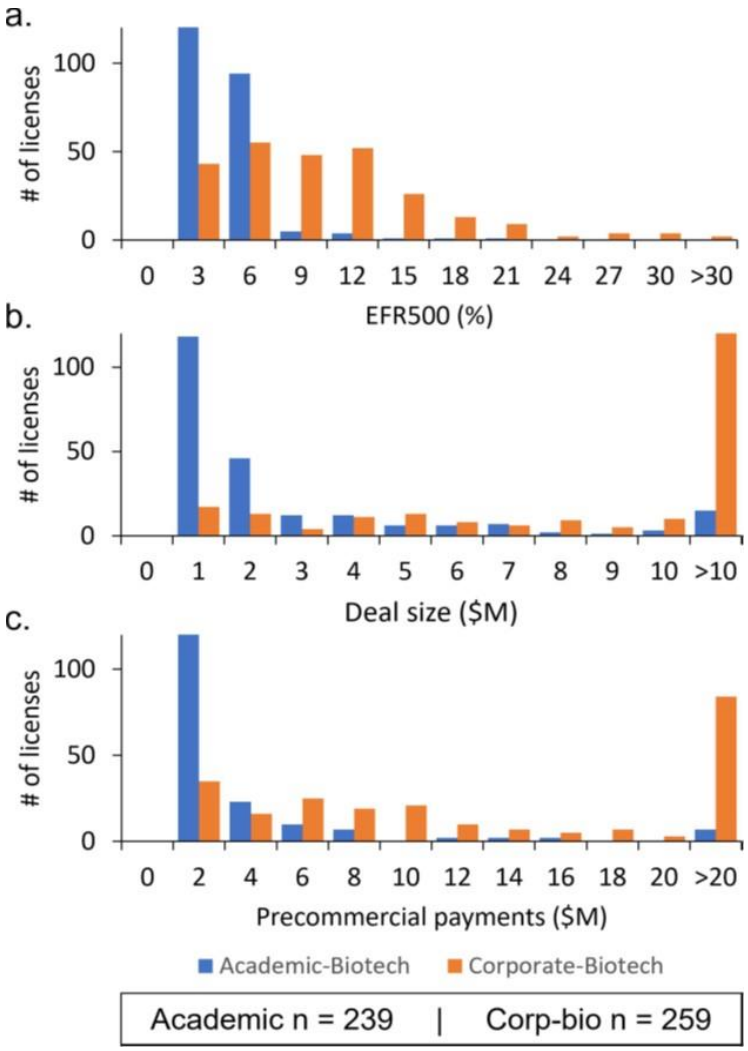

Figure 2. Histogram showing distribution of: (a) effective royalty rate; (b) deal size; and (c) precommercial payments associated with licenses from academic institutions to biotech or between commercial firms. Fom Shah et al (2023) op cit

We call on the NIH to engage in further research directed at establishing the principle that a "reasonable royalty rate" on academic licenses of

[31] 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.

[32] 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.

biotechnologies should not be lower than the rate associated with comparable corporate licenses. This requires greater attention to the reasons that technology transfer offices are not able to negotiate more equitable returns and addressing any systematic deficiencies in the research or licensing process that are identified.[33] It is also necessary to establish the legal principle that the reasonable royalty rate for academic licenses must be comparable to the rates of similar corporate licenses.

3. Impact indicators should be developed that measure the direct, measurable impacts of innovative pharmaceuticals on individuals and their health rather than indirect impacts on economic indicators or broad measures of population health.

Current methods for assessing the impact of technology transfer and the return on government investments in R&D are based largely on economic impact studies and impacts on metrics of employment, productivity, or economic growth. Such metrics, along with population measures of overall morbidity or mortality, do not measure the direct effects of new products on individuals, their state of health, or their wellbeing. Moreover, these methods cannot delineate the impact of individual products. A true measure of the impact of products licensed from academic or government institutions requires new methods that can delineate the impacts of individual products.

We are exploring methods for estimating the "health value" generated by development and dissemination of a specific pharmaceutical product. The method uses established measures of the quality of life gained (measured in Quality-adjusted life years [QALYs]) by use of a pharmaceutical product times the number of individuals using that product. The "value" of improved health is then calculated using a globally adjusted value for the "willingness to pay" (measured in WTP/QALY). Willingness to pay is classically recognized in marketing a mechanism for assessing the value ascribed to a product by an individual. An example of this analysis is shown in Table 3.

Table 3. Health value provided to CMS beneficiaries and US population by treatment with products to treat hepatitis C developed by Gilead Sciences.

		CMS beneficiares				*US population*			
Brand name	**QALY gained**	**individuals benefited**	**Health value**	**Drug spending**	**Residual Health Value**	**individuals benefited**	**Health Value**	**Drug spending**	**Residual Health Value**
Sovaldi	2.61	90,700	$12.1	$8.3	$3.8	156,655	$20.8	$13.1	$7.7
Harvoni	3.26	271,429	$44.5	$23.5	$20.9	388,105	$63.7	$33.4	$30.2
Epclusa	3.94	126,619	$24.0	$7.2	$16.8	176,332	$33.6	$9.0	$24.6
Total		*488,748*	$80.5	$39.1	$41.5	*721,093*	$118.0	$55.5	$62.4

All $ values in billion USD inflation adjusted to 2016. Health Value is calculated using a globally adjusted willingness to pay (WTP) of $52,619.4/QALY (Kouakou and Poder, 2022). Product names: Sovaldi (sofosbuvir); Harvoni (ledipasvir-sofosbuvir); Epclusa (sofosbuvir and velpatasvir). Data sources. QALY data represents average QALY gained compared to no antiviral treatment identified through literature review. Number of individuals benefited obtained from Market Information Data Analytics System (MIDAS) or Centers for Medicare & Medicaid Services (CMS). Reference: Chaves da Silva, P, Conti, R, Ledley FD (unpublished data).

This example estimates the "health value" generated by use of three drugs for treating hepatitis-C developed by Gilead Sciences. In this experiment, the number of QALY gained by an individual using the product is expressed relative to individuals not receiving antiviral drugs.

[33] Various postulated rationale are discussed in Shah et al (2023) op cit.

The results are expressed in two ways. First: total health value represents the number of QALY gained by taking the product times the number of individuals treated (benefiting) times a globally adjusted WTP of $52,619/QALY.[34] Second, the residual health value is calculated by subtracting the price paid for these drugs (i.e. retail price including Medicare out of pocket, or insurance). The results demonstrate the total health value realized by patients under Medicare Part D was >$80 billion with a residual health value of >$41 billion. Nationwide, the total health value realized through use of these products was >$118 billion with a residual health value of >$60 billion. While these studies are in their early stages, we would note that these results are not typical and reflect the value of drugs that cure a significant, endemic disease and have been made widely available through donations and emergence of generic products. These early results suggest it will be possible to directly measure the health value to individuals of novel pharmaceutical products in addition to the broad economic benefits to society. We encourage NIH to further support development of direct measures of pharmaceutical innovation on health.

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[34] Kouakou CR, Poder TG. Willingness to pay for a quality-adjusted life year: a systematic review with meta-regression. The European Journal of Health Economics. 2022 Mar;23(2):277-99. https://link.springer.com/article/10.1007/s10198-021-01364-3