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**Comments of Nikhil Chaudhry, BA, Melissa Barber, PhD, Anthony So, MD, MPA, Ravi Gupta, MD, MS, Joseph S. Ross, MD, MHS, and Reshma Ramachandran, MD, MPP, MHS on the Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights, National Institute of Standards and Technologies (NIST), United States Department of Commerce. 88 FR 85593, Agency/Docket Number: Docket No.: 230831-0207**

Dear Secretary Raimondo, Secretary Becerra, and Under Secretary Locascio:

We write to express our support for strengthening and finalizing the *Interagency Guidance Framework for Considering the Exercise of March-In Rights*. This policy marks an important step forward in ensuring that health technologies developed with taxpayer dollars are available on reasonable – including affordable – terms. Previously, we commented on a prior draft guidance framework, concerned that proposed changes would weaken the federal government’s ability to mitigate the barriers that high prices pose for patients to accessing prescribed and necessary treatments.<sup>1</sup> We now applaud the Administration for drafting a guidance framework that, when determining whether march-in rights should be exercised, considers health technology price and, specifically, when a commercialized product benefitting from federal government support is priced unreasonably for the public.

In our capacity as researchers and physicians at the Yale Collaboration for Regulatory Rigor, Integrity, and Transparency (CRRIT), we continue to be deeply concerned about inequitable access to health technologies including drugs, vaccines, and other medical products. In response to the questions raised in NIST’s proposed guidance, we have put forward some key considerations for further shaping and developing this important policy.

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<sup>1</sup> Ramachandran, R, Gupta R, Ross, JS. Comments of Reshma Ramachandran, MD MPP, Ravi Gupta, MD and Joseph S. Ross, MD MHS on the Department of Commerce’s National Institute of Standards and Technology (NIST) on changes in regulations related to the Bayh-Dole Act governing “Rights to Federally Funded Inventions and Licensing of Government Owned Inventions.” (FR Document #2020-2758) <https://www.regulations.gov/comment/NIST-2021-0001-13420>. Published April 5, 2021.

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**(1) After reading through the framework and example scenarios, if needed, how could the guidance about when an agency might want to exercise march-in and the factors that an agency might consider be made clearer?**

This guidance makes an important contribution in clarifying that price should be a factor in considering “reasonableness.” We strongly support including price as a factor in assessing reasonableness but are concerned that the proposed guidance may be insufficiently operationalizable without additional clarity on factors to consider in determining whether terms – including price—are reasonable or not.

***(a) This guidance provides much-needed clarity on how to interpret affordability within the requirement of “reasonableness”.***

The current draft guidance describes the “foundation of Bayh-Dole's policies and objectives reflect two themes (among others): promoting the development of new products in the U.S. and their availability to end-users or consumers in the U.S.” The legislative history of Bayh-Dole makes clear that affordability was considered a factor in the latter theme of availability to end-users: march-in rights were intended in part to provide protection against abusive pricing.<sup>2-3</sup>

The 1980 legislation included a more forceful range of safeguards to ensure public availability: 35 U.S.C. § 202(c)(7) prohibited the granting of exclusive licenses in some contexts in excess of the earlier of 5 years from first commercial sale or 8 years from the date of exclusive licensing.<sup>4</sup> While this safeguard was removed in the 1984 amendments, it suggests that stronger measures than those currently under discussion in this guidance were considered necessary and desirable by legislators.<sup>5</sup>

Bayh-Dole provisions on march-in rights (35 U.S.C. § 203) enumerate four conditions that should be considered by the federal agency that funded the invention in determining whether licenses should be granted. “Reasonable” appears in the first two conditions:

- (1) “*action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use;*” [emphasis added]

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<sup>2</sup> March-In Rights Under the Bayh-Dole Act. Congressional Research Service. <http://sgp.fas.org/crs/misc/R44597.pdf>. Published August 22, 2016. Statement of Jerome H. Reichman Bunyan S. Womble Professor of Law Duke University School of Law Durham, North Carolina 27708; Peter S. Arno and Michael H. Davis, “Why Don’t We Enforce Existing Drug Price Controls? The Unrecognized and Unenforced Reasonable Pricing Requirements Imposed Upon Patents Deriving in Whole or in Part from Federally Funded Research,” 75 Tulane Law Review (2001); Whalen R. The Bayh-Dole Act & public rights in Federally Funded Inventions: Will the agencies ever go marching in. *Nw. UL Rev.* 2014;109:1083.

<sup>3</sup> Some account of the legislative history of Bayh-Dole (e.g. Rabitschek and Latker 2005) have emphasized Senator Bayh’s *Washington Post* op-ed in response to Arno and Davis (2001), arguing that pricing was not intended to be considered. However, others have noted Senator Bayh argued himself in *CellPro* that price should be considered as a factor in determining reasonable terms (See Bayh’s statement reproduced, *Birch Bayh’s competing interests and evolving views*). The sum of evidence suggests Bayh’s recollections of the legislation’s intent varied and should not be interpreted to exclude the recollection and record of others that price was considered as related to the aims of the legislation. Statement available at: <https://www.keionline.org/21970>. Published August 24, 2012.

<sup>4</sup> Public Law 96-517, Chapter 30—Prior Art Citations to Office and Reexamination of Patents. <https://uscode.house.gov/statutes/pl/96/517.pdf>. December 12, 1980.

<sup>5</sup> Public Law 98-620, Trademark Clarification Act of 1984. <https://uscode.house.gov/statutes/pl/98/620.pdf>. November 8, 1984.

Note: 35 U.S.C. § 201(f) defines *practical application* as “such conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on *reasonable terms*.”

(2) “*action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees.*”

To date, the National Institutes of Health (NIH) and the Department of Health and Human Services (HHS) are the only federal agencies to have received march-in rights petitions. At least eight have been filed for six unique health technologies (petitions for Norvir/ritonavir and Xtandi/enzalutamide were submitted twice), all of which have been denied.<sup>6</sup> Uncertainty in how to define “reasonableness” was a factor in deciding Norvir/ritonavir (2004 and 2012),<sup>7</sup> Xalatan/latanoprost (2004),<sup>8</sup> and Xtandi/enzalutamide (2016 and 2021).<sup>9,10,11</sup>

**(b) Price has been considered in determinations of “reasonableness” in other contexts related to government licensing.**

The plain meaning of “*reasonableness*” as involving some consideration of price has been clearly used in other licensing contexts by federal agencies.

- (1) From 1989 – 1995, NIH had a “reasonable pricing clause” in Cooperative Research and Development Agreements (CRADAs), requiring that there should be “*reasonable relationship between the pricing of a Licensed Product, the public investment in that product, and the health and safety needs of the public.*”<sup>12-13</sup>
- (2) In a 2023 public letter to vaccine manufacturers, HHS Secretary Becerra requested “*reasonable*” prices and suggested that proposed price increases amounted to “*price gouging behavior.*”<sup>14</sup>

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<sup>6</sup> Thomas JR. March-In Rights Under the Bayh-Dole Act. *Congressional Research Service*. <https://sgp.fas.org/crs/misc/R44597.pdf>. Published August 22, 2016.

<sup>7</sup> NIH Office of the Director. Letter In The Case of NORVIR Manufactured by ABBOTT LABORATORIES, INC. <https://www.techtransfer.nih.gov/sites/default/files/documents/policy/March-In-Norvir.pdf>. Published July 29, 2004.

<sup>8</sup> Zerhouni EA. In the case of Xalatan, Manufactured by Pfizer, Inc.

<https://www.ott.nih.gov/sites/default/files/documents/policy/March-in-xalatan.pdf>. Published September 17, 2004.

<sup>9</sup> Letter to Dr. Andrew S. Goldman on Xtandi March-In Rights. <https://www.keionline.org/wp-content/uploads/Final-Response-Goldman-6.20.2016.pdf>. Published June 7, 2016.

<sup>10</sup> Final Response Letter to Representative Doggett on Xtandi March-In Rights. <https://www.keionline.org/wp-content/uploads/Final-Response-Goldman-6.20.2016.pdf>. Published June 20, 2016.

<sup>11</sup> NIH Office of the Director. Final Rejection Letter to Robert Sachs and Clare Love on Xtandi March-In Rights. <https://www.keionline.org/wp-content/uploads/NIH-rejection-Xtandi-marchin-21march2023.pdf>. Published March 21, 2023.

<sup>12</sup> NIH. Notice of Rescinding Reasonable Pricing Clause. <https://www.techtransfer.nih.gov/sites/default/files/documents/pdfs/NIH-Notice-Rescinding-Reasonable-Pricing-Clause.pdf>. Published April 11, 1995.

<sup>13</sup> Hardy LM. Article 5.04 of the Model PHS Exclusive Patent License Agreement. In Institute of Medicine (US) Roundtable for the Development of Drugs and Vaccines Against AIDS. Government and Industry Collaboration in AIDS Drug Development: Summary of a Workshop Held on May 6, 1994. *Washington (DC): National Academies Press (US)*. 1994. HISTORICAL PERSPECTIVES ON GOVERNMENT TECHNOLOGY TRANSFER POLICY AND THE PHARMACEUTICAL INDUSTRY. <https://www.ncbi.nlm.nih.gov/books/NBK231433/>.

<sup>14</sup> Secretary Xavier Becerra, HHS. Letter to COVID-19 Vaccine Manufacturers. <https://www.hhs.gov/about/news/2023/07/13/letter-covid-19-vaccine-manufacturers.html>. Published July 13, 2023.

- (3) In December 2023, the Administration for Strategic Preparedness and Response (ASPR) announced they had successfully negotiated “fair pricing” clauses in their development and production contracts with various companies under Project NextGen, both for several vaccine candidates as well as a treatment for COVID-19.<sup>15</sup>

***(c) Prices for some federally supported inventions are so high as to be considered unavailable on “reasonable terms” and/or not “reasonably satisfy” health or safety needs.***

We will not attempt in this comment to comprehensively describe a vast and growing literature documenting the United States’ exceptionally high drug prices and the resulting morbidity and mortality when patients cannot afford their medicines. Briefly, we note some key findings.

- (1) Launch prices in the United States are the highest in the world. Between 2008 and 2021, new drug launch prices increased by 20% each year and between 2020 and 2021, nearly half (47%) of new drugs were launched at price higher than \$150,000 per year.
- (2) List prices for the 10 prescription drugs initially selected by the Centers for Medicare and Medicaid Services (CMS) for negotiation are three to eight times higher than prices in Australia, France, Japan, United Kingdom, Canada, Germany, and Switzerland.<sup>16</sup>
- (3) Prescription drug prices in the United States were on average nearly double prices that of France and Britain in 2018.<sup>17</sup>
- (4) R&D costs for the 15 drug companies producing the top 20 drugs by sales worldwide cannot explain higher drug prices in the United States; in the year analyzed in the study (2015) net prices for these drugs in the United States exceeded that of other countries by a margin of \$116 billion, more than the total, combined global R&D budget of these companies of \$76 billion that year.<sup>18</sup>
- (5) Vulnerable patients such as older adults in the United States have greater difficulty than patients in other high-income countries accessing prescribed medications due to price.<sup>19</sup>

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<sup>15</sup> The White House. FACT SHEET: Biden-Harris Administration Announces Dozens of Pharma Companies Raised Prices Faster than Inflation, Triggering Medicare Rebates. <https://www.whitehouse.gov/briefing-room/statements-releases/2023/12/14/fact-sheet-biden-harris-administration-announces-dozens-of-pharma-companies-raised-prices-faster-than-inflation-triggering-medicare-rebates/>. Published December 14, 2023.

<sup>16</sup> Gumas ED, Huffman P, Papanicolas I, Williams RD. How Prices for the First 10 Drugs Up for U.S. Medicare Price Negotiations Compare Internationally. *The Commonwealth Fund*. <https://www.commonwealthfund.org/publications/2024/jan/how-prices-first-10-drugs-medicare-negotiations-compare-internationally>. Published January 4, 2024.

<sup>17</sup> Robbins R and Jewett C. Six Reasons Drug Prices Are So High in the U.S. *NY Times*. <https://www.nytimes.com/2024/01/17/health/us-drug-prices.html>. Published January 17, 2024.

<sup>18</sup> Yu NL, Helms Z, Bach PB. R&D Costs for Pharmaceutical Companies Do Not Explain Elevated US Drug Prices. *Health Affairs Blog*, March 7, 2017. DOI: 10.1377/hblog20170307.059036

<sup>19</sup> Ramsay C and Williams RD. Medicare Patients Pay More for Drugs Than Older Adults in Other Countries; Congress Has an Opportunity to Move Forward. *The Commonwealth Fund*. <https://www.commonwealthfund.org/blog/2021/medicare-patients-pay-more-drugs-older-adults-other-countries-congress-has-opportunity>. Published September 30, 2021.

(6) Being forced to miss doses or being unable to fill prescriptions due to price has also been found to be associated with worse health outcomes, including increased risk for hospitalization, and worsening functional status.<sup>20</sup>

***(d) One of the strengths of this guidance is it provides some foundation for consistency across federal agencies, as march-in determinations have historically been made at agency discretion and with no right of appeal for the petitioner. While we support the clear articulation that price should be considered in assessments of reasonableness, how price should be considered leaves considerable room for uncertainty.***

(1) The guidance addresses to a limited degree how price should be evaluated:

(i) Under subheading *Is a statutory criterion met*, the guidance notes:

*“If the contractor or licensee has commercialized the product, but the price or other terms at which the product is currently offered to the public are not reasonable, agencies may need to further assess whether march-in is warranted. Whether action may be needed to meet the needs of the Government or protect the public against nonuse or unreasonable use of the subject invention may include consideration of factors that unreasonably limit availability of the invention to the public, including the reasonableness of the price and other terms at which the product is made available to end-users.”*

(ii) The guidance further defines “reasonableness” under subheading *Is a statutory criterion met*, Criterion 2, factor V:

*“Is the contractor or the licensee exploiting a health or safety need in order to set a product price that is extreme and unjustified given the totality of circumstances?*

*A. For example, has the contractor or licensee implemented a sudden, steep price increase in response to a disaster that is putting people’s health at risk?*

*It should be noted that in reviewing this question, the agency is not limited to reviewing price increases; the initial price may also be considered if it appears that the price is extreme, unjustified, and exploitative of a health or safety need.”*

(2) The scenarios suggest a further set of principles to consider:

(i) Intent to profiteer: *“If the evidence suggests this 1000% increase was an intentional act by the company to “cash- in” on this newly discovered health and safety need, that would weigh in favor of march-in.”* (Scenario 5)

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<sup>20</sup> Williams CP, Davidoff A, Halpern MT, Mollica M, Castro K, Allaire B, de Moor JS. Cost-Related Medication Nonadherence and Patient Cost Responsibility for Rural and Urban Cancer Survivors. *JCO Oncology Practice*. 2022 Aug; 18(8). doi: <https://doi.org/10.1200/OP.21.00875>

- (ii) Substantial price increases (here 400%), assuming the agency has ruled out increases in the cost of manufacture. (Scenario 6)
- (3) One shortcoming of the guidance is while articulating that high initial prices may be a factor supporting a decision to ‘march-in’, the scenarios posed only describe situations with price increases. Scenarios and/or analysis should be provided with guidance for how to evaluate absolute prices, and not just price increases. Moreover, another consideration for use of march-in rights might also be substantial price increases or price gouging in the settings of a stockout or shortage.
- (e) *The current guidance provides that price should be considered a factor but would be improved by enumerating factors for consideration in determining whether a price is “extreme”, “unjustified”, “exploitative”, or “appropriate” when considering exercising march-in rights.*

We recognize the challenges of drafting guidance that is general enough to be appropriate for a wide range of agencies and technologies, and still sufficiently specific as to be operationalizable. While the principles identified in (d) are a useful starting point, we propose that the guidance should enumerate further ‘factors for consideration’. As our expertise in in health technologies, we focus on factors appropriate in this domain.

There is precedent for several methodologies to assess the “reasonableness” of a health technology price.

- (1) External reference pricing: prices in the United States are compared to a set of defined comparator countries.  
Precedent: Recent draft legislation on negotiated development and purchasing contracts with the federal government have included a “most favored nation” clause that required pharmaceutical manufacturers to charge the U.S. government the lowest price among G7 countries.<sup>21,22</sup>
- (2) Cost plus pricing: assess the cost of the product (cost of production, or cost of production and product development, depending on the circumstance) and add a profit margin consistent with comparable technologies.  
Precedent: The Department of Defense uses cost plus contracts.<sup>23</sup> A bipartisan US Senate inquiry considered cost of production in assessments of insulin pricing practices.<sup>24</sup> AstraZeneca and Johnson & Johnson received more than \$1.5 billion in federal support for COVID-19 vaccine development and committed to participating in Operation Warp Speed on

<sup>21</sup> Pandemic and All-Hazards Preparedness Act Senate HELP Committee Draft Bill 2023. [https://www.help.senate.gov/imo/media/doc/pahpa\\_discussion\\_draft.pdf](https://www.help.senate.gov/imo/media/doc/pahpa_discussion_draft.pdf).

<sup>22</sup> Chaudhry N, Ramachandran, R. Reasonable Pricing Clauses: A First Step Toward Ensuring Taxpayers a Fair Return on their Public R&D Investment. *Bill of Health*, Petrie-Flom Center for Health Law Policy, Biotechnology, and Bioethics, Harvard Law School. <https://blog.petrieflom.law.harvard.edu/2023/09/28/reasonable-pricing-clauses-a-first-step-toward-ensuring-taxpayers-a-fair-return-on-their-public-rd-investment/>. Published September 28, 2023.

<sup>23</sup> GAO. Defense Acquisitions: Assessments of Selected Weapon Programs. <https://www.gao.gov/assets/gao-08-467sp.pdf>. Published March 2008.

<sup>24</sup> Documents Produced by Sanofi for U.S. Senate. [https://www.finance.senate.gov/imo/media/doc/Sanofi\\_Redacted.pdf](https://www.finance.senate.gov/imo/media/doc/Sanofi_Redacted.pdf). Published 2019.

a nonprofit basis (it should be noted that these commitments were neither adhered to nor enforced.)<sup>25</sup>

- (3) Cost-effectiveness analysis, for example through quality-adjusted life years (QALYs): assessing the benefit of a given technology to a benchmark or a comparator. QALYs are “a measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the quality of life. One quality-adjusted life year (QALY) is equal to 1 year of life in perfect health.”<sup>26</sup>

Precedent: Health Technology Assessments (HTA) were developed by the U.S. Office of Technology Assessment in the 1970s.<sup>27</sup> The National Center for Health Care Technology (NCHCT) developed methodologies like QALYs to evaluate the comparative utility of different health technologies.<sup>28</sup> Measures of cost-effectiveness are also used by the US Preventive Services Task Force.<sup>29</sup>

- (4) Evidence of unavailability and unaffordability: evidence might include patient surveys, analyses of catastrophic expenditures, market penetration, evidence of rationing by individuals or within public health systems,<sup>30</sup> and formulary inclusion.

***(f) NIST should remove guidance suggesting that the availability of an alternative therapy – even an inferior one – should be considered a factor in not using march-in rights.***

- (1) The guidance discusses consideration of alternative therapies in both statutory discussion and scenarios.
- (i) Under heading *Is a statutory criterion met?*, Criterion II, D, VI.  
*“How would march-in address the health or safety need? Are there other products, or other potential alternatives to march-in, that would address the health or safety need, in whole or in part?”*
- (ii) Under heading *Would march-in support the policy & objective of Bayh-Dole, considering the specific case and broader context?*, section II, A:  
*Are there other alternatives available to address the problem identified? How effective are the alternatives (or how likely is it*

<sup>25</sup> Brennan, Z. Vaccine-makers’ ‘no profit’ pledge stirs doubts in Congress. *Politico*. <https://www.politico.com/news/2020/07/13/vaccine-makers-profit-congress-360135>. Published July 13, 2020.

<sup>26</sup> National Institute for Health and Care Excellence. Glossary. <https://www.nice.org.uk/glossary?letter=q>.

<sup>27</sup> Banta, D, Jonsson, E. History of HTA: Introduction. *Cambridge University Press*. 2009 Jul; 25 (S1). doi: <https://doi.org/10.1017/S0266462309090321>.

<sup>28</sup> Office of Technology Assessment. Development of Medical Technology, Opportunities for Assessment. *Washington, DC: US Government Printing Office*. Published 1976.

<sup>29</sup> Saha S, Hoerger TJ, Pignone MP et al. The art and science of incorporating cost effectiveness into evidence-based recommendations for clinical preventive services. *Am. J. Prev. Med.* 20(3 Suppl.), 36–43 (2001).

<sup>30</sup> Florko, N. Hundreds of incarcerated people are dying of hep C — even though we have a simple cure. *STAT News*. <https://www.statnews.com/2022/12/15/hundreds-incarcerated-people-dying-hepatitis-c-despite-simple-cure/>. Published December 15, 2022.

*that other alternatives would solve the problem), and how effective are the alternatives in comparison to march-in?*

(iii) Scenario 3:

*“For example, are there other products that could support the market need while the contractor increases its production capacity? Alternatives need not be superior to the subject invention to be a consideration weighing against march-in.”*

- (2) We could not identify where in the statute or any legislative intent the guidance draws its consideration that availability of inferior treatment can be considered to satisfy need. One of the four conditions for march-in rights states that *“action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees.”* We appreciate there is some nuance here: a vaccine with 89% effectiveness can be seen as reasonably satisfying a health need relative to a vaccine with 90% effectiveness. However, a comparator vaccine with 20% effectiveness cannot be considered to have alleviated health need.
- (3) We strongly submit that consideration of alternative therapies should only be considered if the alternative therapy is wholly interchangeable. Factors in determining ‘wholly interchangeable’ may include:
  - (i) Effectiveness: the alternative is comparably effective or more effective
  - (ii) Indications: the alternative has been approved for all indications and patient groups (e.g., considering children, pregnant women, etc).
  - (iii) Drug-drug interactions: more patients are not anticipated to be excluded from the alternative than the comparator.
  - (iv) Side effects: the alternative does not have more side effects that would limit patient utilization.
- (4) In our clinical practice, we find that these conditions would be rarely met for most therapies, except perhaps in cases of different dosage forms (ie, 2 x 2mg tablets vs 4mg tablet formulation).
- (5) Moreover, even when wholly interchangeable alternative therapies are available, it may be the case that even with therapeutic competition, reasonable pricing is absent. Thus, the availability of wholly interchangeable alternative therapies should not itself override the consideration of exercising march-in rights.

***(g) NIST should remove guidance suggesting that price increases for a given product should not be considered if similar products have also experienced price increases.***



- (1) Scenario 6 suggests that price increases for a given product should not be considered if similar products have also experienced price increases:
- “The following week, the consumer goods company increased the price of its masks 100%, and it continued to raise the price over the course of a month, resulting in a 400% price increase. The company has also sent letters to other mask manufacturers, flagging the pending patent application and promising to file lawsuits against any infringers as soon as the patent issues. The agency would first ask the contractor for information to confirm the basic facts—for example, that the contractor has increased price 400%, how that increase compares to prices for other masks, how that price point compares to the cost of developing and manufacturing the masks, that the contractor has filed for patents, and that it is threatening to file suit against competing.”*
- (2) The background of Scenario 6 already makes clear that the agency had assessed costs of developing and manufacturing masks, and presumably not found an increase in these costs to be the driver of cost increases. In such a situation, we do not follow the logic that price increases observed across many mask manufacturers should dissuade the agency from exercising march-in rights on the mask manufacturer under consideration. Such a conclusion is not congruous with empirical evidence of the market conditions that enable price increases without cause (i.e., price increases not resulting from increased costs of production or other exogenous factors). Firms have been documented to coordinate and/or collude to increase prices through at least three mechanisms: (1) explicit collusion to set prices;<sup>31</sup> (2) ‘parallel pricing’ or ‘shadow’ pricing where firms raise prices in lockstep with each other;<sup>32</sup> and (3) supply disruptions that increase pricing power serve as indirect coordination mechanisms.<sup>33</sup> Unexplained price increases within the same market should trigger at the very least antitrust concerns, and should be a factor *supporting* rather than *dissuading* march-in rights, as the health need alleviated will be greater.

***(h) We propose that the guidance should explicitly state that the following factors will not be considered in march-in determinations.***

- (1) The guidance should articulate that only list prices will be considered in price evaluations. Rebates – in addition to being impossible to verify – will only

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<sup>31</sup> James, L. New York And 43 Other States Sue 20 Generic Drug Manufacturers Alleging Conspiracy To Fix Prices And Allocate Markets For More Than 100 Generic Drugs. <https://ag.ny.gov/press-release/new-york-and-43-other-states-sue-20-generic-drug-manufacturers-alleging-conspiracy-fix>. Published May 13, 2019.

<sup>32</sup> U.S. House of Representatives Committee on Oversight and Reform. Drug Pricing Investigation Majority Staff Report. <https://oversightdemocrats.house.gov/sites/democrats.oversight.house.gov/files/DRUG%20PRICING%20REPORT%20WITH%20APPENDIX%20v3.pdf>. Published December 2021.

<sup>33</sup> Weber IM, Wasner E. Sellers’ inflation, profits and conflict: why can large firms hike prices in an emergency?. *Review of Keynesian Economics*. 2023 Apr 14;11(2):183-213.

apply to patients using certain insurance plans and or pharmaceutical benefits managers (PBMs).

- (2) Patient access or assistance programs that provide *ad hoc* coupons should not be considered as satisfying “reasonable terms” of availability or affordability. The agency will not have the means to verify that every patient who cannot afford a given health technology at an unreasonable price has access to products through such programs, and the license holder can cease these programs at any time.
- (3) Criterion II E under heading *Would March-In Support the Policy & Objective of Bayh-Dole, Considering The Specific Case And Broader Context?*, which states “*Consider whether other legal processes (e.g., a challenge to the validity of the patent, licenses being revoked) may allow another manufacturer to bring the product to market more quickly, as that could weigh against use of march-in*” should be removed. Patent challenges are lengthy and uncertain, with the agency in most cases having no information to assess whether the challenge is likely to be successful. This condition would unnecessarily delay exercise of march-in rights.

**(2) The framework contains many terms which have specific meanings under Bayh-Dole or in technology development and commercialization. Are the definitions provided at the beginning of the framework easy to understand? Do they aid in your ability to interpret the framework?**

We have no further comments on the definitions provided at the beginning of the framework.

**(3) How could the framework be improved to be easier to follow and comprehend?**

(a) We do not follow the logic of some of the considerations presented in Scenario 4.

- (1) In this scenario, a flood has interrupted the manufacture of a monoclonal antibody that is the only treatment for a rare disease. The company will not be able to manufacture the antibody until repairs are made, and then an additional 4 months are required to complete manufacturing of a batch.
- (2) In the Discussion, the guidance notes:  
*“The manufacturing problems in this scenario seem largely outside of the contractor’s control. That suggests march-in would be unlikely to resolve non-use or unreasonable use of subject inventions in the future, although it could deter other future collaborators from developing subject inventions, weighing against march-in (Section III).”*
- (3) The scenario clearly states that the factory will be out of commission for an extended period of time. The company will make no revenue on their antibody. It therefore does not follow that the issuance of a march-in right could be understood as

*“deter[ring] other future collaborators from developing subject inventions”*, as in this situation the company loses no revenue from the entry of a competitor until it is able to manufacture a product again.

- (b) There is a typo on page 85599: Under the *Is a statutory criterion met?* heading, the criteria are numbered I, II, III, VI instead of I, II, III, IV.
- (c) There is missing closed quotation mark on page 85600, under heading *Would march-in support the policy & objective of Bayh-Dole, considering the specific case and broader context?*.

*The Bayh-Dole regulations under 37 CFR 401.6(a)(6) state that “[t]he consistency of the exercise of march-in rights with the policy and objectives of 35 U.S.C. 200 shall also be considered. The Bayh-Dole Act emphasizes “utilization of inventions arising from federally funded research and development” and the “commercialization and public availability of” those inventions...*

The missing closed quotation mark after “considered” at the close of the first sentences gives the reader a misleading impression that the second sentence is statutory language. Instead, 37 CFR § 401.6(a)(6) states *“The consistency of the exercise of march-in rights with the policy and objectives of 35 U.S.C. 200 shall also be considered. In cases referred for fact-finding, the head of the agency or designee may reject only those facts...”*

**(4) Does this framework sufficiently address concerns about public utilization of products developed from subject inventions, taking into account the fact that encouraging development and commercialization is a central objective of the Bayh-Dole Act?**

- (a) We are concerned that the section of the guidance addressing concerns about public utilization of products developed from subject inventions is not operationalizable.*

There are many factors for why no march-in petitions have been successful since the passage of the Act. We applaud the introduction of guidance that reduces ambiguity and eases operationalization, but we urge NIST to learn from the lessons of the past (e.g., historic ambiguity over how “reasonableness” should be assessed) and ensure that the draft guidance does not contain elements that are not operationalizable and whose ambiguity might delay or stymie future petitions and require further guidance.

- (b) The policy and objectives of Bayh-Dole (35 U.S.C. § 200) include considerations of the effect of march-in rights on broader innovation policy (“inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise without unduly encumbering future research and discovery”), but the rest of the legislation does not include specific application for how this intent would be made actionable within march-in rights.*

***(c) The guidance requires that Agencies considering march-in petitions should consider broader economic effects. We are concerned that the guidance asks agencies considering march-in petitions to evaluate evidence that is unavailable through frameworks which are poorly and ambiguously defined. For example, it is unclear a) what evidence would be required and b) how the agency would be able to assess:***

- (1) The “*potential impact on the broader R&D ecosystem*” (Criterion III)
- (2) “*Unintended consequences on U.S. competitiveness and innovation*” (Criterion III, A1).
- (3) The degree to which the exercise of march-in rights might “*foster support for the federal research enterprise.*” (Criterion III, B).
- (4) Whether exercise of march-in rights would “*promote competition without unduly encumbering future R&D*” or “*impact competition and R&D more broadly*”. (Introduction of section and Criterion III, C).
  - a. Further guidance is provided here, suggesting that the agency consider whether there would be “*a decrease in the number of applicants for federal funding.*” (Criterion III, C).
- (5) Whether exercise of march-in rights for a given invention would “*have an impact on U.S. competitiveness and innovation?*” (Criterion III, D1).
- (6) Whether “*prospective licensees likely avoid future collaborations with federally funded research institutions, organizations, small businesses, and investigators*” (Criterion III, D2).
  - a. Further guidance is provided here, suggesting that the agency consider if “*there be a decline in the number of collaborations with the federal laboratory? Would an agency’s practice result in a decline in the number of collaborations?*” (Criterion III, D2).
- (7) Whether exercise of march-in rights might have a “*potential chilling effect on the agencies’ existing relationships with industry and ability to address Administration priorities.*” (Criterion III, D2).

***(d) We note with concern some practical challenges to evaluating the guidance in (c) above. In our view, the a) lack of available data for many factors, b) lack of frameworks here or in the literature for evaluating and weighing tradeoffs even where data exist, and c) ambiguity over how the probability of potential effects should inform decision-making make it likely that agencies will find this guidance challenging to operationalize. The evaluation of a single petition should not implicitly require that agencies conduct macroeconomic analysis and modelling of the potential effects of march-in rights in general.***

- (1) This guidance is intended to be used by an agency evaluating a single march-in petition. There are few contexts where the exercise of march-in rights for a single invention might reasonably be expected to have sector-level consequences, let alone the national-level effects on competitiveness and innovation to which the guidance refers. One implication is the guidance tasks agencies with assessing macroeconomic effects of march-in petitions in *general*, while only providing them with frameworks designed for assessing the *specific* circumstances of a given march-in petition.
- (2) It should be emphasized that **a march-in petition has never been successful**. There is therefore little evidence from which agency could predict or model economic effects.
  - (i) Reports of the potential demise of U.S. innovation and competitiveness from march-in rights or comparable actions are, in our view, greatly exaggerated. The guidance suggests far greater certainty than exists in the economics literature that march-in rights would be expected to have wide-ranging effects.
  - (ii) The effects of exercising of march-in rights on innovation should be contextualized within broader federal powers: 28 U.S.C. § 1498 already allows the federal government to license a patent without the permission of the patent holder. March-in rights are important in achieving fair access to the fruits of taxpayer funded federal research, but their exercise does not amount to an exceptional or unprecedented disruption to innovators' perception of risk in capital investments.
  - (iii) The closest comparator of a policy shock is likely the rescinding of "fair pricing clauses" from NIH Cooperative Research and Development Agreements (CRADAs). Studies of the effect of "reasonable pricing clauses" on the number of CRADAs found no evidence of decline.<sup>34</sup>
- (3) Much of the language in this section of the guidance refers to "potential" effects. Implicit in "potential" is a probability distribution of many possible outcomes, with no guidance for how agencies should model, assess, or weigh potential outcomes. For example, how should agencies weigh a small probability of a large negative effect against a large probability of a small negative effect? Few economists would comfortably assert zero effect of any action on markets. The standard of "potential" impacts is unworkable in that agencies will only in highly unusual circumstances be able to assert with certainty that there was no "potential" negative effect to be considered.
- (4) Many of the terms used in Criterion III guidance (e.g. "competitiveness", "innovation", "encumbering future R&D", "chilling effect") do not have standardized measures that would facilitate comparison.

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<sup>34</sup> Sarpatwari, A, LaPidus AK, Kesselheim, AS. Revisiting the National Institutes of Health Fair Pricing Condition: Promoting the Affordability of Drugs Developed with Government Support. *Annals of Internal Medicine*. 2020 Jan. doi: <https://doi.org/10.7326/M19-2576>

- (i) The guidance suggests that agencies “*Consider whether input from other agencies would be helpful to understand the ramifications of a march-in decision, e.g., the State Department, Office of the U.S. Trade Representative, or Department of Commerce as to any diplomatic or trade implications or the United States Patent and Trademark Office as to any intellectual property implications.*” (Criterion III, D2). It is unclear what empirical data these agencies hold that might inform decision-making. The above agencies in some cases have well-known policy preferences – for example the USTR through measures like the Special 301 List has historically opposed any non-voluntary licensing of intellectual property – but such *general* policy preferences should not be anticipated to inform *specific* cases under consideration, as they are divorced from the context of a given case.
- (ii) Even assuming standardized measures existed, and data were available, there is no framework here or more generally in the literature that would allow agencies to weigh a measure of alleviation of health need against a measure of decreased global competitiveness.

*(e) Aim 3 of the guidance is to “encourage the consistent and predictable application of the Bayh-Dole Act’s march-in authority.” Frameworks and criteria that are vague and/or difficult to interpret/implement in practice run counter to this aim by introducing further “black boxes” into decision-making, and thereby maintaining the status quo of agency discretion without clarity or accountability.*

*In sum, we are concerned that the Criterion III “What are the wider implications of use of march-in?” section of the guidance is not fit for purpose and should be removed. Criteria I-II sufficiently address whether the exercise of march-in rights support the policy and objectives of Bayh-Dole.*

**(5) The framework is not meant to apply to just one type of technology or product or to subject inventions at a specific stage of development. Does the framework ask questions and capture scenarios applicable across all technology sectors and different stages of development? How could any gaps in technology sectors or stages of development be better addressed?**

It is unavoidable that any guidance will not be able to cover all aspects of development across a diverse range of technologies. We propose that transparency and accountability are important elements in frameworks that can accommodate diverse contexts with consistency.

*(a) Transparency: We are concerned by restrictions on the transparency of march-in decisions.*

- (1) We agree with concerns raised by Members of Congress, Knowledge Ecology International, and others that the guidance in the footnote in *Regulatory*

*Procedures for March-In* that notes that “All portions of the march-in proceeding are closed to the public and are held confidential (35 USC 202(c)(5))” amounts to a misreading of 35 U.S.C. § 202(c)(5), which only requires that information on the “utilization or efforts at obtaining utilization” are to be treated as commercial and financial information and not subject to disclosure.

- (2) We also note that even if information were deemed to be commercial or financial information, “federal regulators generally do have a legal right to disclose (and thereby “break”) even *bona fide* trade secrets. This authority emerges from the regulators’ enabling statutes and from the fundamental background principle, formalized in statutes and reaffirmed by the Supreme Court, that federal agencies have legal discretion to disclose information within their possession.”<sup>35</sup>
- (3) Stakeholders in march-in rights petitions, including Members of Congress, have urged the NIH and HHS to hold public hearings.<sup>36</sup> Public hearings would allow stakeholders to engage publicly with the agencies on this issue. To date, the agencies have not hosted such a hearing, instead engaging with petitioners as well as the contractors or licensees through private meetings.

***(b) Accountability: the evidence put forward by the licensee and the evaluation of evidence by the agency should be as transparent as practicable, and other mechanisms to ensure accountability should be considered.***

- (1) The march-in process relies on a) the full and honest disclosure of evidence by the licensee and b) a high level of technical expertise by the agency fact-finder to accurately assess evidence. This may not be practical as the agency cannot be reasonably expected to have expertise over all federally funded technologies.
- (2) There is no right of appeal by the petitioner. Legal scholars have proposed that the petitioners be granted an appeal right;<sup>37</sup> contractors are already granted appeals through 37 C.F.R. § 401 and can appeal decisions in the United States Court of Federal Claims (35 U.S.C. § 203(b)). Other proposed mechanisms to remedy the present procedural imbalance between petitioner and contractor also include a centralized “second look service” undertaken by NIST to ensure “that there is a check on the currently unchecked discretion that agencies enjoy in deciding whether or not to commence a march-in proceeding.”<sup>38</sup>
- (3) An accountable process demands that the public – at the very least – be afforded the opportunity to identify where evaluations might have been made on the basis of incomplete or inaccurate evidence.

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<sup>35</sup> Morten, C. Publicizing Corporate Secrets. *U. PA. L. Rev.* 2023;171:1319-1404.

[https://scholarship.law.upenn.edu/cgi/viewcontent.cgi?article=9816&context=penn\\_law\\_review](https://scholarship.law.upenn.edu/cgi/viewcontent.cgi?article=9816&context=penn_law_review).

<sup>36</sup> U.S. Congress. Letter to Secretary Becerra on March-In Rights.

<https://www.warren.senate.gov/imo/media/doc/Bicameral%20Xtandi%20Petition%20Follow-up%201.10.23%20FINAL1.pdf>. Published January 10, 2023.

<sup>37</sup> Whalen R. The Bayh-Dole Act & public rights in Federally Funded Inventions: Will the agencies ever go marching in. *Nw. UL Rev.* 2014;109:1083.

<sup>38</sup> *Ibid.*

## **Relevant Experience\***

**Nikhil Chaudhry, BA** is a Postgraduate Associate at the Yale Collaboration for Regulatory Rigor, Integrity, and Transparency. He completed his undergraduate studies at Emory University in May 2023, receiving a Bachelor of Arts in Biology and Human Health. Prior to joining CRRIT, Nik was a Health Policy Intern at New America and Intellectual Property Litigation Intern at Kilpatrick Townsend & Stockton. Nik is currently working on public comments and policy engagement.

**Melissa Barber, PhD** is postdoctoral fellow at Yale Law School and Yale School of Medicine (joint appointment). Her research focuses on drug access and pharmaceutical markets. She completed her doctorate at Harvard University in 2023 in the Department of Population Health Sciences and has served as a consultant on pharmaceutical issues for the World Health Organization (WHO), Médecins Sans Frontières (MSF), the Global Fund to Fight AIDS, Tuberculosis, and Malaria, and the World Bank.

**Anthony D. So, MD, MPA** is Distinguished Professor of the Practice and Director of the Innovation+Design Enabling Access (IDEA) Initiative based at the Johns Hopkins Bloomberg School of Public Health. He has written on the strategic use of intellectual property rights for global health as part of a commissioned paper for the Institute of Medicine's Committee on the U.S. Commitment to Global Health, on "Making Intellectual Property Work for Global Health" in the *Harvard International Law Journal*, and on the question, "Is Bayh-Dole Good for Developing Countries? Lessons from the U.S. Experience," in *PLoS Biology*. He has also served on the Institute of Medicine Committee on Accelerating Rare Disease Research and Orphan Product Development, on the Working Group on Antibiotic Resistance for the U.S. President's Council of Advisors on Science and Technology, as Co-Convener of the UN Interagency Coordination Group on Antimicrobial Resistance delivering recommendations to the UN Secretary-General in 2019, on the Technical Advisory Groups of the WHO's COVID-19 Technology Access Pool and WHO's Market Information for Access to Vaccines program, and as Co-Chair of the technical working group on aligning incentives for pharmaceutical innovation to achieve fair pricing for the 2021 WHO Fair Pricing Forum. He also serves on the Board of Public Citizen and the Advisory Council of the Universities Allied for Essential Medicines.

**Ravi Gupta, MD, MS** is a physician and health policy researcher. He is an Assistant Professor in the Division of General Internal Medicine at Johns Hopkins Medicine. Ravi's work focuses on strengthening FDA regulation and improving prescription drug policy with an emphasis on intellectual property, anti-competitive behaviors, and ensuring affordability and access to safe and effective therapies, both in the U.S. and abroad.

**Joseph S. Ross, MD, MHS**, is a Professor of Medicine (General Medicine) and of Public Health (Health Policy and Management) at the Yale School of Medicine, an Associate Physician of the Center for Outcomes Research and Evaluation at Yale-New Haven Health System, and Co-Director of the National Clinician Scholars Program at Yale. He also co-directs the Yale Collaboration for Regulatory Rigor, Integrity, and Transparency (CRRIT). A practicing general internist with expertise in health services and outcomes research, his research examines the use



and delivery of higher quality care and issues related to pharmaceutical and medical device regulation, evidence development, postmarket surveillance, and clinical adoption.

***Reshma Ramachandran, MD MPP, MHS*** is a family medicine physician, health services researcher, and Assistant Professor at Yale School of Medicine. She co-directs the Yale Collaboration for Regulatory Rigor, Integrity, and Transparency (CRRIT). One of her research focus areas is around examining the impact on patient health outcomes of publicly granted incentives along the drug development pipeline to pharmaceutical companies. On October 25, 2012, in her prior role as a fellow with the American Medical Student Association, she partnered with Knowledge Ecology International, U.S. Public Interest Research Group, and Universities Allied for Essential Medicines in filing a march-in rights petition for the anti-retroviral drug, ritonavir.<sup>39</sup> On October 17, 2016, she also sent a letter of support on behalf of the National Physicians Alliance and 10 other non-governmental organizations to NIH Director Francis Collins urging the agency to exercise march-in rights as petitioned earlier by Knowledge Ecology International and the Union for Affordable Cancer Treatment.<sup>40</sup> She serves as Board President for Universities Allied for Essential Medicines North America and as Chair of the FDA Task Force for Doctors for America.

**\*Institutional affiliations are for identification purposes only; the views expressed are those of the individual only, not of any institution noted.**

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<sup>39</sup> Love J. 2012 October. Four NGOs ask NIH to grant open licenses to ritonavir patents under Bayh-Dole March-in provisions. Knowledge Ecology International. Published October 25, 2012. <https://www.keionline.org/22023>

<sup>40</sup> Struver Z. 11 Groups Urge NIH to Lower Price of Xtandi, NIH/Army-Funded Prostate Cancer Drug With \$129k/Year Price Tag. Knowledge Ecology International. Published March 22, 2016. <https://www.keionline.org/23041>