UNIVERSITIES ALLIED FOR ESSENTIAL MEDICINES

The Honorable Gina Raimondo
Secretary of Commerce
Washington, DC 20230

The Honorable Laurie E. Locascio
Under Secretary of Commerce for Standards and Technology
Washington, DC 20230

**Universities Allied for Essential Medicines comments in support of Docket No.: 230831-0207: "Request for Information Regarding the Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights"**

Universities Allied for Essential Medicines (UAEM) thanks NIST and the interagency working group for the opportunity to comment on this draft guidance. Our comment focuses on support for the approach outlined in the draft guidance, and focuses on particular details within the framework in criterion 1, 2, and 3. We also address questions raised in the draft guidance. UAEM submits this comment in the context of application to health technologies including drugs, biologics, and medical devices.

**Background and Relevant Expertise**

UAEM is a global network of students and recent alumni advocating for affordable access to medicines discovered with public funding on university campuses. In 2001, students at Yale University were alerted to the price of an HIV/AIDS medicine called stavudine (d4T), which was discovered on campus. The medicine was licensed exclusively to Bristol Meyer-Squibb and priced at over $10,000 per person, per year in some regions. Students put public pressure on the university and the company, and convinced them to return to the drawing table on their license. This licensing agreement lowered the cost of stavudine to below $1.00 per day. UAEM was founded by the students who led this effort, and became the first and only organization solely focused on access provisions in the patenting and licensing practice of inventions discovered on university campuses.

Over the years, UAEM has worked with universities around the world to implement global access licensing principles, frameworks for access licensing, and innovative affordable action plans. These plans and licensing agreements put in place terms that protect access and affordability of licensed medical products. According to our Global Health Grades report card in 2020, 22% of surveyed universities were using these types of agreements in the United States.[1]

Outside of university-specific licensing policies, UAEM has been party to multiple requests for march-in rights use under the Bayh-Dole Act. On October 25, 2012, UAEM filed a march-in

[1] See our white paper: https://globalhealthgrades.org/wp-content/uploads/2021/03/UAEM-2020-U.S.-University-Report-Card-White-Paper_final.pdf

petition with Knowledge Ecology International (KEI), the American Medical Students Association (AMSA), and the U.S. Public Interest Research Group (U.S. PIRG), requesting the National Institutes of Health (NIH) issue a license for Abbott's patent on ritonavir. Ritonavir was discovered and brought to practice through funding from the National Institute of Allergy and Infectious Diseases (NIAID). This request was denied by the NIH, wherein the director acknowledged that pricing concerns may exist for ritonavir, but claiming that they were not sufficient to trigger a march-in at that time.[2]

In early 2022 UAEM, joined Knowledge Economy International (KEI) and others in a petition sent to the Department of Health and Human Services secretary Xavier Becerra to request the use of march-in to bring down the price of Xtandi a late stage prostate cancer drug.[3] Xtandi is priced three to five times higher in the United States when compared to other high income countries, with prices for a single 40 mg capsule running from $66 to more than $100 a capsule.[3] According to the FDA "orange book" the three patents listed for Xtandi have disclosed public funding through the US military and the NIH.[3] For cases such as Xtandi, where the federal government, and as an extension the American public have a had in the creation of such a health technology, the Bayh-Dole act serves as an mechanism to serve the interests of the public through maximizing public utilization of such inventions. However in March of 2023, the NIH declined this request "march-in" citing that UCLA had done a sufficient job in ensuring public use of the drug.[4] These assessments did not take into consideration unmet health needs and reasonableness of price as a condition to march-in. The case of Xtandi and similar health inventions remains relevant and the use of march-in right would support the objective of the

The NIH's reluctance has been driven by a lack of clarity about how a reasonable price would be determined and what factors would be used to do so. This draft guidance seeks to build a framework for that decision, and thus, UAEM supports this framework and the inclusion of price as a factor for triggering march-in rights.

**Addressing the Innovation Canard**

Opponents to march-in rights use, access licensing provisions, reasonable pricing, or negotiation have been using the same arguments since the passage of Bayh-Dole. They claim that changing the system will stymie innovation. A cornerstone of this argument rests on a surface-level assessment of Cooperative Research and Development Agreements (CRADAs).

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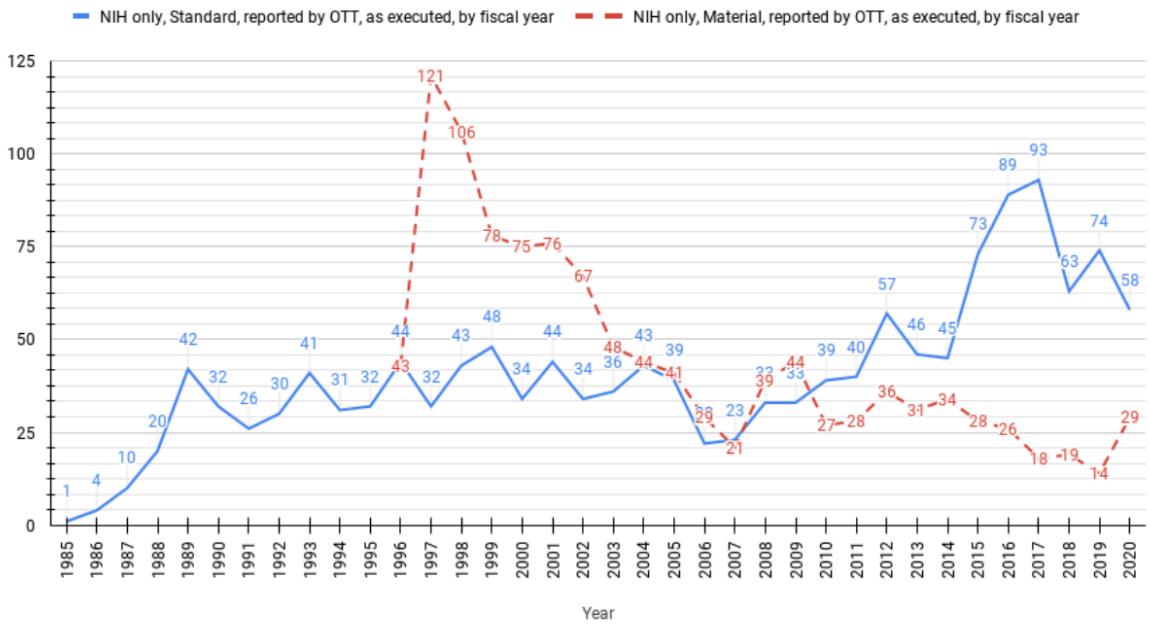
[2] See NIH response letter: https://www.keionline.org/wp-content/uploads/Norvir_NIH_Signed_Determination_1Nov%202013.pdf

[3] Xtandi: 2021-2022 Request to US Department of Health and Human Services to Use the US Government's Rights in Patents. (n.d.). Knowledge Ecology International. Retrieved January 29, 2024, from https://www.keionline.org/xtandi2021

[4] NIH-rejection-Xtandi-marchin-12march2023.pdf. (n.d.). Retrieved January 30, 2024, from https://www.keionline.org/wp-content/uploads/NIH-rejection-Xtandi-marchin-12march2023.pdf

Their claim is that after the removal of reasonable pricing clauses in CRADAs in 1995,[5] the number of these agreements with the private sector increased, resulting in fewer signed contracts when the NIH utilized a reasonable pricing clause in their agreements. But, as documented by Knowledge Ecology International,[6] this interpretation of CRADAs ignores a key factor – the NIH began issuing a new type of CRADA, called the material CRADA in 1997 in addition to changing the reasonable pricing language, accounting for the change.

**Figure 1: NIH Standard and Material CRADAs, reported by OTT as executed, by fiscal year**




Simply put, the data shows that rather than reasonable pricing terms holding back CRADA uptake, the new CRADAs just drew in more contractors overall. Meanwhile, standard CRADA uptake remained steady before and after the removal of reasonable pricing clauses.

**Suggestions to Further Develop Criterion from the Framework**

> ***Criterion 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;*

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[5] Leary, W. 1995. U.S. Gives Up Right to Control Drug Prices, NYT. At: https://www.nytimes.com/1995/04/12/us/us-gives-up-right-to-control-drug-prices.html

[6] Love, J. 2021. The number of standard and material CRADAs executed by the NIH from 1985 to 2020 and the relationship to NIH reasonable pricing clause. https://www.keionline.org/wp-content/uploads/KEI-BN-2021-3.pdf

Criterion 1 implies that we should expect a reasonable time for a contractor or assignee to take steps toward application of a patented product. Correctly, the interagency framework has identified that reasonable times will depend on the application of the product, the field of use for it, and other factors that will not be identical across all product portfolios. However, we submit that timelines for practical application should be defined and publicized.

We strongly support the intention behind this criterion. Product shelving is a critical issue that can have detrimental effects on the health and safety of the public. Product shelving has had effects on medicines in recent years. In 2004, Gilead Sciences allegedly shelved HIV therapies to maximize earnings on a previously existing version of the medication, despite that drug being associated with kidney and bone issues. The company has faced a series of lawsuits brought by patients and others concerned with the shelving of these products.[7] UAEM asserts that a clear march-in trigger related to shelving could help curb this behavior in the future.

Of course, extenuating circumstances may exist that could force a contractor or assignee to miss their intended practical application. Under those circumstances, the agency should be able to consider extensions on a case-by-case basis in accordance to what stage of development a technology is in.

> ***Criterion Point 2:*** *Action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees.*

UAEM supports a broad interpretation of "health and safety needs" ranging from the affordability of a medication to ensuring access to necessary medication in times of national emergency.

Under criterion 2, question V, the guidance asks, "is the contractor or the licensee exploiting a health or safety need to set a product price that is extreme and unjustified, given the totality of circumstances?"

UAEM specifically supports this criterion and finds it in line with price gouging legislation that exists across many states and is active during a state of emergency. In fact, legislation often sets a percentage-based increase, comparing prices before and after an emergency order is issued, and empowers Attorneys General to go after price gougers with steep civil and criminal penalties. Utilizing march-in as a possible remedy for price gouging on a product that was developed with public funding would be in alignment with existing price gouging remedies.

> ***Criterion Point 3:*** *Action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees.*

[7] https://www.fiercepharma.com/premium/webinar/unleashing-ai-opportunities-strong-data-foundation

As indicated in comments we jointly submitted with Public Citizen and others to this same docket, we recommend using international reference prices as one possible approach to determine reasonable pricing for march-in rights. However, we recognize that there could be many thresholds utilized for reasonable pricing, and have identified a few options, including:

- Criteria as suggested by the Prescription Drug Price Relief Act of 2019 (PDPRA). According to the PDPRA thee price for a drug is considered excessive "if the domestic average manufacturing price exceeds the median price for the drug in Canada, the United Kingdom, Germany, France, and Japan…if pricing information is unavailable…the price is still considered excessive if it is higher than reasonable in light of specified factors, including cost, revenue, and the size of the affected patient population."[8]
- Standards set by prescription drug affordability boards in Maryland, Maine, Oregon, Colorado, and in consideration in Illinois, Michigan, Ohio, and other states. These boards review the costs of medicines under patent that are priced at $30,000 or more, face a price increase of 10% or more, and pose an affordability issue for patients who take it.[9] A similar threshold could be used for march-in rights consideration to be in alignment with multiple states.
- Utilize thresholds for price increases that trigger the Medicaid drug rebate program, which caps price increases based on an inflation-based calculation.[10]

Beyond reasonable price, UAEM urges the interagency guidance to consider affordable access to health technologies of interest to vulnerable, underserved, and special needs populations in the U.S., as defined by the Department of Health and Human Services. The University of California, Berkeley utilizes language in licensing agreements as a part of it's affordable access plan provision, and this language could be utilized as a model for information requested during a march-in proceeding.[11]

The interagency proposal states a caveat that relies on leaving the pricing criterion for march-in rights up to the "good faith" of the market in the scenarios section. This is counterintuitive in that there is no substantial plan put forth by the proposal to check that the market changes are due to natural causes. Additionally, such terminology does not hold when the market is susceptible to pharmaceutical company's price gouging. No entity holds the responsibility of such a task, thus ultimately undermining any progress made towards providing the public with a clear stance. The interagency draft guidance includes a statement of intent to "develop a comprehensive framework" to address how such checks would work. We urge the interagency working group

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[8] Sen. Sanders, B. [I-V. (2019, January 10). S.102 - 116th Congress (2019-2020): Prescription Drug Price Relief Act of 2019 (2019-01-10) [Legislation]. https://www.congress.gov/bill/116th-congress/senate-bill/102

[9] See for example: https://www.nashp.org/wp-content/uploads/2019/04/Final-Prescription-Drug-Affordability-Review-Board-QA-4_1_2019.pdf

[10] https://www.medicaid.gov/medicaid/prescription-drugs/medicaid-drug-rebate-program/index.html

[11] View here: https://ipira.berkeley.edu/sites/default/files/shared/docs/EXCL%20EQUITY%20therapeutics%20diagnostics%2007April2023.pdf

make developing this framework a priority to ensure actions for and against industry are well-informed and represents the interest of the America public.

**Answers to specific questions**

> *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?*

It is UAEM's view that the biggest clarifications needed for the exercise of march-in rights are around a reasonable timeline for a product to begin development toward it's practical use, and in setting standards for reasonable prices for products developed with taxpayer funds.

> *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?*

UAEM suggests expanding on one section of the definitions, potentially defining this term or at least making reference to where this term can be further defined.

Practical Application—To manufacture in the case of a composition or product, to practice in the case of a process or method, or to operate in the case of a machine or system; and, in each case, under 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.

The phrase "reasonable terms," if left undefined, leaves open the same ambiguity that has allowed for march-in rights to be underutilized to begin with. We suggest considering referencing thresholds set in the final framework to define "reasonable" in this section.

**Conclusion**

UAEM supports the draft Interagency Guidance Framework for Considering the Exercise of March-In Rights with the inclusion of our critiques as outlined above. We believe this framework is an important step to fulfill the objectives of the Bayh-Dole Act, and bring great benefit to the American public.

*UAEM is available for further discussion by contacting our executive director, Justin Mendoza, at justin@uaem.org or 269-888-4453.*

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