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January 29, 2024

The Honorable Dr. Laurie Locascio
Director
National Institute of Standards and Technology
100 Bureau Drive
Gaithersburg, MD 20899

RE: Request for Information Regarding the Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights [NIST-2023-0008]

Dear Dr. Locascio,

The American Academy of Neurology (AAN) is the world's largest neurology specialty society representing more than 40,000 neurologists, clinical neuroscience professionals, and students. The AAN is dedicated to promoting the highest quality patient-centered neurologic care. A neurologist is a doctor with specialized training in diagnosing, treating, and managing disorders of the brain and nervous system. These disorders affect one in six people and include conditions such as Alzheimer's disease, stroke, migraine, multiple sclerosis, concussion, Parkinson's disease, and epilepsy.

The AAN thanks the National Institute of Standards and Technology (NIST) for the opportunity to provide feedback on the agency's Request for Information Regarding the Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights, 88 Fed. Reg. 85593, (Dec. 8, 2023) (RFI). The march-in rights established by the Bayh-Dole Act[1] represent a meaningful lever at the Administration's disposal to address the exorbitant prices of drugs developed with the aid of public funding. Many of the most expensive drugs on the market treat life threatening neurological conditions, for which there are limited therapies available. The AAN is interested in strategies to ensure both access and affordability for neurologic therapies for all patients who need them.

Addressing the high burden of drug costs for neurology patients is a key priority for the AAN. Action must be taken to ensure that prescription medications are accessible for patients with complex chronic neurologic conditions. Potential solutions should be simple and transparent and should make pharmaceutical medications more affordable for patients. Cost containment efforts must also address the burden on the entire health care system as high prescription drug prices may be shifted and absorbed in ways

[1] Bayh-Dole Act, 35 U.S.C. §§ 200-212 (1980).

that negatively impact patient and prescriber access to important medications. Neurologists often rely on pharmaceuticals to treat or manage their patients' conditions, many of which are considered rare diseases. Many of these therapies are the direct result of publicly funded neurological drug development research. Accordingly, the AAN is highly supportive of continued public funding for research for neurological disease treatment and has an interest in policies that may impact the development of, or market access to innovative therapies.

High drug costs pose numerous challenges for neurology patients, primarily by potentially limiting access to treatment. The annual cost of treating neurologic disease in the United States exceeds $500 billion, and prescription drugs for neurologic conditions are some of the most expensive on the market.[2] Recent data also indicates that out-of-pocket costs for neurologic drugs have increased considerably in recent years.[3] Drugs that treat complex, chronic conditions like Parkinson's disease, epilepsy, and migraine, and specialty drugs which may require special handling or administration, such as those used for multiple sclerosis, are particularly expensive. Spending on specialty medications has increased by $54 billion since 2011 and now accounts for more than 70 percent of all prescription spending growth.[4] These prices directly impact patients and their treating providers as they work together to treat neurologic illness.

Request for Information

NIST has requested input from the public on the Administration's proposed framework for an agency to exercise its march-in rights for certain patented inventions under certain circumstances. Under the Bayh-Dole Act, a private contractor may hold the patent for an invention resulting from the collaboration and use of public and private funds, but the Federal Government maintains march-in rights. These rights allow the agency that provided the public funding to require the contractor to license the invention to other entities under certain circumstances. One area of focus of this RFI is whether and how an invention's exorbitant price can trigger march-in rights.

The AAN recognizes the complexity of the proposed march-in framework and the onerous task of administering this process. The AAN recognizes that there is a distinct problem associated with exorbitantly high drug prices impeding patient access that is not as acute in other markets. Given that many neurologic conditions such as Alzheimer's disease, epilepsy, migraine, and multiple sclerosis among others are chronic conditions, neurology patients with chronic conditions are affected by high drug prices for years. In addition, we believe this is particularly noteworthy and requires action due in part to the contributions that federally funded research has made to the development of many high-priced neurologic medications. Within the current drug development ecosystem, there is a need for greater accountability for pharmaceutical manufacturers to set reasonable prices for medications that

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[2] Callaghan, Brian, et al. Position Statement: Prescription Drug Prices. American Academy of Neurology, https://www.aan.com/siteassets/home-page/policy-and-guidelines/policy/position-statements/18_prescriptionpricesps_v304.pdf.

[3] Callaghan, Brian C, et al. "Out-of-Pocket Costs Are on the Rise for Commonly Prescribed Neurologic Medications." Neurology, Lippincott Williams & Wilkins, 28 May 2019, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6556089/.

[4] IMS Institute for Healthcare Informatics. Medicines Use and Spending in the U.S. – A Review of 2015 and Outlook to 2020. Accessed January 18, 2017. http://www.imshealth.com/en/thought-leadership/ quintilesims-institute/reports/medicines-use-and-spending-in-the-us-a-review-of-2015-and-outlookto-2020

have benefited from taxpayer-funded research. The AAN applauds the framework's objective of ensuring affordable and accessible treatments for Americans and supports the judicious use of march-in rights to address the ultra-high cost of drugs, noting that we have previously supported policies that have tied the use of federal funding in drug development to ensuring that prices paid by patients are not exorbitant.

Although the AAN is supportive, the AAN is concerned that the proposed framework has ambiguities that can potentially lead to inconsistent interpretation, unfair application, and legal disputes, which may hinder patient access to therapy. The AAN believes that efforts to lower drug prices would be most effective if the framework limits the potential for discretion and institutionalizes a thoroughly systematic process wherein inventions and factors—including pharmaceutical prices paid by patients—are evaluated consistently against clear standards, which should be included in public-industry agreements at the inception of the collaboration. The AAN appreciates that there are significant access and equity concerns that regulators and industry participants must consider when determining the price of pharmaceuticals. Further, the AAN recognizes that any regulatory intervention of this nature to address the high cost of pharmaceuticals will likely lead to protracted litigation.

High drug prices are a complex issue that has caused limitations on patient access. March-in rights, if used to successfully reduce the price of a drug, will not address many other barriers to access that patients face today. We encourage the Administration to consider additional strategies to ensure patient access, including reform to prior authorization and step therapy rules, efforts to promote greater transparency across the pharmaceutical supply chain, more consistent consideration of median U.S. income with respect to both pharmaceutical prices and out of pocket costs to patients, and additional efforts to promote competition in the marketplace.

In response to the NIST's RFI to seek insight and perspectives to inform the agency's proposed framework on the use of march-in rights, the AAN and its members have responded to select questions and recommend the policy changes outlined below to ensure that decision making related to march-in meets the purpose of promoting patient access to innovative therapies, as well as the objectives of the Bayh-Dole Act.

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?***

While the proposed march-in framework and example scenarios present how an agency would approach the decision to use march-in rights, the subject inventions and attributes that bring these inventions in-scope require additional clarification. Section 201 of the Bayh-Dole Act[5] and the RFI both provide definitions for "funding agreements" and "subject inventions," and together these definitions provide a description of what inventions could be subject to march-in rights. The RFI goes on to discuss challenges in determining whether an invention is within the scope of march-in rights, particularly whether the contractor reported the invention to the government. It is unclear what the impact of an unreported subject invention would be on an agency's ability to use march-in rights. The framework could be further

[5] §§ 201(b), (e).

improved by a statement that clearly presents the necessary conditions taken from the appropriate definitions for a product to be in scope.

The AAN appreciates the financial investment and risk involved in drug research and understands that financial remuneration is an important incentive underpinning research for innovative therapies. For that reason, the AAN is concerned that the lack of clear and objective criteria to determine whether the price of a particular product is unreasonable would lead to inconsistent application of march-in rights. Without standard criteria or factors for identifying a reasonable price, it is possible that an agency may fail to consider or undervalue critical factors contributing to the price, leading the agency potentially take action that may unduly result in limiting patient access. In addition, we believe that establishing clear standards for reasonable prices could create conditions in which pharmaceutical companies set prices that make their products more accessible for patients before march-in rights need to be invoked.

2. How could the framework be improved to be easier to follow and comprehend?

The proposed framework discusses drug prices being a factor favoring march-in rights but does not differentiate between public and private payers. The AAN notes that beneficiaries covered by different payers may face different prices for the same drug. To aid the agency's analysis to determine whether a price is unreasonable, more transparency is needed regarding the variation in price across payers and the factors that contribute to the price or prices being analyzed under the framework. We also would encourage the agency to assess patients' out-of-pocket costs under different types of insurance coverage and to consider whether those out-of-pocket costs are feasible in light of patients' income.

Even with public funding, pharmaceutical research and development involves a significant financial risk to the organization undertaking that research. While the framework and scenarios illustrate circumstances when march-in would be appropriate, there is little discussion on circumstances when a high cost is reasonable or when other factors are present that disfavor march-in rights. Additionally, the RFI presents many considerations for an agency to include in its analysis. These considerations do not present firm or objective rules that agencies must adhere to, and we are concerned that without clear standards and rules for administering march-in rights, key considerations could be inconsistently applied.

The RFI states that exorbitant prices are not enough to justify march-in rights without other factors present, and the scenarios that address high costs include additional factors that favor march-in. These are very helpful in understanding how cost and other factors can support march-in action. We would recommend additional scenarios that showcase more factors and considerations that, when combined with an exorbitant cost, favor march-in, especially cases directly relating to pharmaceutical prices.

3. 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?

The AAN is concerned that the use of march-in rights may cause a short-term supply chain disruption for necessary medication during the transfer of a license. We recommend that the agency acknowledge this risk and ensure the terms of any licensing agreement do not impact the patent-holder's ability to produce the subject invention or result in a temporary shortage. A central policy objective of the Bayh-Dole Act is to support innovation, and the financial incentive of marketing and selling a drug is often a central factor driving research and development. The AAN is concerned that the use of march-in rights, regardless of justifying factors and reasonableness, could have a chilling effect on future neurological drug development research—especially for potential pharmaceutical products whose research and development was supported with public funding. We recommend that relevant agencies exercise march-in rights judiciously and in a limited manner to ensure that patient access to innovative therapies is not detrimentally impacted. The AAN believes that manufacturers may respond proactively to the potential use of march-in as described under the framework and hopes that the release of this framework serves the purpose of exerting downward pressure on exorbitantly priced therapies.

Additionally, many neurology patients rely on pharmaceuticals to treat rare diseases, and these new drugs are often developed and tested by small biotech companies. March-in may negatively impact this sector of drug development and the willingness to engage in research targeting rare diseases if the framework under which march-in rights are considered fails to consider market size when considering a particular product's price. We ask the agency to give special consideration to the value of ensuring continued innovation for therapies treating rare diseases to ensure that future collaboration with the private sector is not inappropriately hampered.

The RFI framework contains criteria that depend on whether the contractor has acted reasonably to commercialize an invention. Reasonableness may be interpreted differently between agencies and regulators, which could lead to inconsistent application of this framework. To alleviate the burden on regulators of determining whether a price is reasonable and to promote consistent and unbiased evaluation under the framework, the AAN recommends the formation of a committee comprised of public and private sector participants to review, analyze, develop, and issue recommendations regarding the appropriateness of exercising march-in rights in cases identified by relevant agencies. We would encourage the public sector participants to be representatives from multiple federal agencies, including NIH, FDA, and CMS.

Conclusion

The publication of this draft framework represents this Administration's commitment to lowering drug prices for Americans. It is the hope of the AAN that the potential utilization of march-in rights will cause drug manufacturers to consider the factors affecting the price of their products and lead to equitable solutions that value the investment made in research and development while supporting patient access and affordability.

The AAN appreciates the opportunity to provide a response to this Request for Information. The AAN is committed to working with regulators to increase access to life-saving pharmaceuticals and to promote the continued research and development of treatments for

neurological diseases. Please contact Matt Kerschner, the AAN's Director, Regulatory Affairs and Policy at mkerschner@aan.com or Cale Coppage, the AAN's Senior Government Relations Manager at ccoppage@aan.com with any questions or requests for additional information.

Sincerely,

Carlayne E. Jackson, MD, FAAN
President, American Academy of Neurology