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Laurie E. Locascio
Director and Undersecretary of Commerce for Standards & Technology
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February 6, 2024

RE: Request for Information Regarding the Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights

Dear Director Locascio:

Thank you very much for this opportunity to respond, on behalf of myself and others, to the Draft Interagency Guidance Framework on potential use of the government's "march-in" rights under the Bayh-Dole Act. I write to object generally to the Draft Guidance and specifically to its proposed exercise of march-in rights under 35 U.S.C. § 203 to issue licenses to patents on subject inventions if the funding government agency deems such exercise appropriate based on factors "*including the reasonableness of the price and other terms at which the product is made available to end-users*."

The Draft Guidance would address all technological developments falling under the purview of the Bayh-Dole Act and could therefore have wide-ranging and likely unforeseen and unintended consequences. The Draft Guidance appears to be focused on reducing biopharmaceutical prices, but it will instead have far reaching effects on a vast array of businesses and technologies across the U.S. economy. Other commenters will doubtless explain the inevitable and unintended but vast harms it would inflict on the U.S. innovation economy and the government's ability to play a constructive role in supporting it.

We write instead to address the apparently *intended* effects of the Draft Guidance on biopharmaceutical prices, which are both misguided in conception and certain to fail in execution. The Draft Guidance will not achieve its aims, and any effects it has on biopharmaceutical innovation will be harmful at best. Thus, its unintended consequences make the Draft Guidance even more ill-advised, producing little gain but much pain.

The Draft Guidance clearly is motivated by the desire to reduce biopharmaceutical prices, despite its breathtaking reach. The Draft Guidance itself mentions drug prices a number of times. Perhaps more indicative of the impetus behind the Draft Guidance is the fact that all eight of the march-in petitions filed under the Bayh-Dole Act thus far were addressed to the NIH, and all eight objected to the prices of particular pharmaceutical products or to the licenses to their patents. Those who have long advocated this theory of price-based march-in rights (discredited and rejected until now) have been frank in their desire to limit exclusive rights in biopharmaceuticals and reduce their prices.

Although the Draft Guidance is quite detailed and multifactorial, it is in the end far too simplistic an

approach to the incredibly complex reality of pharmaceutical development, distribution, and pricing in the U.S. Indeed, there are good reasons to question whether The Draft Guidance would have any real effect on biopharmaceutical prices at all. For many of those same reasons, exercising Bayh-Dole march-in rights based on "the reasonableness of [drug] prices" could have a negative effect on the continued development of government-funded basic research into safe, effective, and administrable biopharmaceutical products.

The Draft Guidance is unlikely to achieve its goals of influencing drug prices

As a first matter, there is little evidence or reason to believe that exercising march-in rights on patents to government-funded inventions alone would yield any influence over biopharmaceutical prices. Very few drugs have active patents subject to march-in. A recent study by health technology consultant Vital Transformation shows that, of the 361 novel, non-generic, small-molecule and biologic drugs that had unexpired patents listed in the FDA's Orange Book or Purple Book between 2011 and 2020, only 8% had patents that contained "government interest statements" or other indications of at least partial funding under a federal research grant or government contract.

Of those drugs with patents potentially subject to march-in, even fewer are covered by only government-funding associated patents. The Vital Transformation study cohort included only five (1.3%) drugs that had *only* government funding associated patents listed. Even then, the study did not distinguish between composition of matter patents and method of use patents. This means that potentially fewer than one percent of the drugs in the studied cohort would be subject to patent rights sufficient to influence ultimate drug pricing.[1] Other academic studies support this conclusion – although publicly funded research has contributed greatly to the identification of biological targets and even new molecular entities (NMEs) with potential for pharmaceutical use, less than ten percent of those NMEs were patented by public sector institutions.[2]

In other cases, patents on any related government-sponsored research may have expired or be nearing expiration by the time any potential applications of that research reach their intended end-users. Although government-funded researchers rely on patents to attract initial investment into developing their research further, the long development cycles in many science-based technologies such as biopharmaceuticals often means that those early basic research patents will have little to no patent term remaining by the time a useable product is developed. Exercising march-in rights on such expired patents again would leave government agencies with no leverage over drug prices.

Another major question is whether a government agency could effectively achieve anything by using its march-in rights to grant a "license to [a] subject invention to a responsible applicant or applicants." So far, march-in right petitioners have almost uniformly been unable to produce drugs themselves. In the eight march-in petitions filed with the NIH, the petitioners were almost never those capable of producing the drug in question. Instead, they were nonprofit organizations, patient groups, or members of Congress. (The exception was CellPro, which in its 1997 petition asked the NIH to march-in on patents owned by Johns Hopkins but licensed to a competitor after CellPro rejected the licensing terms the competitor offered). It was not clear if either the NIH or the petitioners in any given case had identified a suitably qualified biopharmaceutical manufacturer who could step in not only to receive the license but also to practice the subject invention.

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[1] Composition of matter patents are typically the broadest and therefore the most valuable rights to a biopharmaceutical because method of use patents can easily be circumvented through "off-label" prescribing practices. And although some studies of government funding associated patents on biopharmaceuticals include methods and devices for manufacturing, screening, detecting, and other aspects related to drug development, these types of patent rights are even less likely to offer much control over ultimate drug pricing.

[2] Ekaterina Galkina Cleary et al., *Contribution of NIH Funding to New Drug Approvals 2010–2016*, 115 PNAS 2329 (2018).

Even if a biopharma manufacturer were to receive a license as a result of march-in, it is not necessarily easy for manufacturer to step up to the plate. This challenge has become greater given the increasingly reliance on biologics, which work wonders but are the product a complex web of innovation rather than a simple "recipe." Biologics are notoriously difficult to reproduce and often require specialized equipment, expertise, and facilities to produce. Indeed, this is the reason that the Biologics Price Competition and Innovation Act (BPCIA) does not even require manufacturers to demonstrate that their follow-on biologics are identical to the reference biologic that they are seeking to emulate – rather, the BPCIA requires only that the follow-on be biosimilar to the reference biologic. And even generics will often face difficulties in reproducing any given small-molecule drug.

Also, marching in on a single government-funding related patent will often fail to enable copying. As noted above, most new drugs, particularly biologics, are subject to multiple patent rights (some licensed from third parties), not just those to which a government agency might have march-in rights. Thus, even though an agency might grant a generic or biosimilar manufacturer a license to those few patents subject to march-in rights, there may remain a number of other unexpired patents that may need to be licensed from the private sector or litigated. Again, march-in rights provide no assurance that a particular drug product can be manufactured at all, much less at a lower price than its original manufacturer offers.

The Draft Guidance simultaneously undermines incentives to invest in developing public sector research into biopharmaceuticals

More generally, any proposal to use Bayh-Dole march-in rights to regulate drug prices fails to uphold the policy and objectives of the Bayh-Dole Act. Prior to enactment of Bayh-Dole, government-funded research often languished on the shelf because private industry was unwilling to invest in the development of unpatented technologies; just prior to Bayh-Dole, less than five percent of the tens of thousands of patents the federal government owned at the time were ever licensed. Earlier, a 1968 GAO Report to Congress found that hundreds of new drug compounds developed by government-funded labs went unscreened by pharma companies because they could not secure their investment with exclusive rights. A policy correction to allow patenting and licensing ended this wasteful and counterproductive outcome, and the Bayh-Dole Act later made these changes permanent.

The use of march-in rights to regulate drug prices, however, fails to take into consideration the true costs of developing drugs – not just the costs of basic research or even the costs of *inventing* drugs themselves, but also the clinical trials necessary to obtain regulatory approval to use the drugs on patients. Without a thorough understanding of the full cost of drug development, exercising march-in rights on biopharmaceutical patents could have damaging effects on the industry's incentives and even ability to continue to develop more drugs from public sector research.

For example, sofosbuvir (Sovaldi), a breakthrough treatment for chronic hepatitis C infections, has often been cited as a drug developed largely through government grants and yet sold at what many saw as exorbitantly high prices. The invention of sofosbuvir was indeed the result of many long years and millions of dollars of government-funded basic research by a number of academics, but before the drug could be approved by the Food & Drug Administration, it had to go through several more years and millions – or perhaps billions – of dollars of clinical trials testing to ensure that the drug is safe and effective enough for use in patients. This final but essential step appears to have been privately funded, with perhaps only a $250 thousand Qualifying Therapeutic Discovery Grant, according to a 2015 Senate Committee on Finance report. Exactly how much companies on average invest in R&D and clinical trials is hotly debated, but to assert that, because public funding contributed to some early part of the development of a drug, the government must necessarily wield its march-in rights to regulate drug prices, ignores the economics of biopharmaceutical development.

Of course, simply exercising march-in rights is not the same as invalidating or banning public sector biopharmaceutical patents – under the use of march-in, biopharmaceutical companies still have the

opportunity to earn some return on their investments. Nonetheless, the call to use march-in rights to control drug prices seems to be based on the belief that the innovators within the pharmaceutical industry earn far too much profit on their efforts and that the government therefore should use its powers to lower domestic drug prices. In the absence of robust and accurate data proving that excessive profits are the rule, however, the governmental efforts run the very real risk of damaging the U.S. pharmaceutical industry.

First, as noted above, this belief this ignores the immense costs of developing pharmaceuticals, particularly those truly new pharmaceuticals that are most likely to be subject to march-in petitions because no "me-too" versions, generics, or follow-on biosimilars have yet entered the market and exerted downward pressure on drug prices.

Second, to the extent that the profitability of pharmaceutical innovation is relevant, it must be based on rigorous, objective, and *long-term longitudinal* studies of net earnings that pharmaceutical innovators earn. This requires more than focusing on the net returns on particular pharmaceutical *products* (and not just pharmaceutical *substances*) or even on a company's entire catalog of products at any given point in time. According to the pharmaceutical industry's own reporting, less than a third of the products that actually reach the market even earn sufficient revenue to recoup their research and development costs. This means that the 30% or so of products that are "flagship" offerings must compensate not only for their own R&D costs but also the R&D costs of the remaining 70% or so of products whose net revenues are negative.

Moreover, the minority that are flagship products also must compensate for the far larger number of products that never reach the market because they are not safe or effective enough for use or otherwise fail to achieve regulatory approval. Finally, while any one company may earn enough on their flagship products to earn a net profit overall, even after taking into account products with net negative revenues and products that failed, those net positive overall earnings can shift dramatically for the negative. These changes in net earnings occur frequently when companies face "patent cliffs" (loss of patent protection) on currently profitable flagship drugs with no new flagship drugs in the near-term pipeline, or when a company faces liability for regulatory violations, product flaws, etc.

At this point in time, however, we have highly conflicting reports biopharmaceutical profits that vary across such a large range of estimates that it is difficult to form a reliable impression of exactly how much drug prices could be altered before decreasing the rate at which the U.S. biopharmaceutical industry can continue innovating and developing new products. Furthermore, the one result that does seem fairly predictable is that the using march-in rights to control drug prices would deter private industry from using publicly funded patents as foundations for new and socially beneficial biopharmaceuticals.

Thank you very much for your time and consideration of this letter.[*]

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