

KEI Comment 3: Request for Information Regarding the Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights (NIST–2023–0008)

Topic: The guidance needs to explain what “available to the public on reasonable terms” means, in practice.

Introduction	1
Extreme, unjustified and exploitative isn’t the right standard	1
International price comparisons	2
Restrictive tiers on insurance formularies should trigger a review	3
Revenue milestones	3
Access in developing countries	4
Complex Patent Landscapes	4
Administrative and judicial appeals, injunctions and stays	5
ANNEX Pricing Clauses in U.S. Government Contracts for COVID-19 Products	6

Introduction

The draft guidance gives several examples of factors that may be considered when evaluating the merits of a march-in case. Some of the examples are unhelpful, important topics are missing, and there is a lack of attention given to solutions to known challenges, such as complex patent landscapes.

While KEI is pleased to see that the draft guidance clarifies that pricing is a factor in march-in cases, on the issue of standards for unreasonable pricing, the draft guidance gets a failing grade.

Extreme, unjustified and exploitative isn’t the right standard

The draft guidance includes this discussion, which set off alarm bells for everyone trying to lower drug prices.

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.

Several really bad and unhelpful standards are included in this section of the guidance.

First, why lead with “sudden steep” price increases, which do happen (such as the 2003 Norvir 400 percent price increase, cited in the unsuccessful 2004 march-in case) but are rare, and when the high rollout prices and steady annual price increases are the primary problem?

Second, is the Biden Administration really saying that a price needs to be “extreme, unjustified, and exploitative of a health or safety need” in order to be addressed? Does a candidate drug have to check all three boxes?

There are products with high prices that are available because they are reimbursed by government programs and private insurance. But that does not mean the price is reasonable.

I agree that sudden steep price increases, or prices that are extreme (whatever that means in today’s world of sky’s-the-limit prices), unjustified (based upon what standard?) and exploitative of a health or safety need” (taking advantage of mandatory placement on formularies or being a treatment without equivalent substitutes?) are bad. But in more than 13,000 words, there does not seem to be any actual guidance on what is reasonable, extreme, unjustified or exploitative.

More to the point, what happened to “available to the public on reasonable terms,” the language in the statute and the one quoted in the legal analysis? How do we get from reasonable to not extreme, unjustified and exploitative?

International price comparisons

The guidance asks “At what price and on what terms has the product utilizing the subject invention been sold or offered for sale in the U.S.?” One elephant in the room is the comparison between what US residents and taxpayers pay for a product, and what residents of other high income countries pay. This is hardly a fringe issue. All of the previous march-in requests that raised pricing issues make comparisons to foreign prices. This was central to the Norvir, Xalatan and Xtandi march-in cases, and a theme in countless politicians’ campaign rhetoric including both President Biden and former President Trump. President Trump even issued an executive order to use an international reference price as a ceiling on Medicare pricing.

One can argue whether or not International Reference Pricing caps make sense in general for the United States, given the size of our market, but for a federally funded invention it should be used as a presumed maximum price. If anything, US residents should pay less for inventions they funded, but certainly not more.

It is not necessary to have a rigid standard that has no exceptions. But the burden should be on the drug company to justify charging US residents more than other residents of other high income countries.

If the Biden Administration was serious about guidance on march-in cases and drug prices, it would choose a reference pricing model and set out the factors to consider if a company wants an exception to justify charging US residents a higher price.

Among the issues to address are which countries are in the standard, do you use the mean or the best price, and do you adjust the prices for relative per capita incomes?

For which countries to include, we recommend picking a group of 7 to 11 of the largest economies by GDP that have at least 50 percent of the US GDP.

This is hardly a radical standard. Pfizer signed a contract on Paxlovid pricing for most favored nation pricing. Pfizer agreed to the lowest price for a “Covered Nation” which it defined as “a nation that is a member of the Group of Seven (Canada, France, Germany, Italy, Japan, the United Kingdom, and the United States) plus Switzerland.” Several other countries also signed pricing clauses relating to COVID-19 products, as are described in the Annex.

Restrictive tiers on insurance formularies should trigger a review

If products end up on restrictive tiers for health insurance, that should trigger a review to see if a march-in is required. Full stop. In the review a patent holder could argue that there is a justification for a price that creates the unfavorable placement on formularies, but the burden needs to be on the company whose taxpayer-funded invention is priced so high access is narrowed by restrictive formularies.

Revenue milestones

Beyond an International Reference Price cap, which just deals with discrimination against US residents, are revenue milestones.

For some product, particularly for products with large markets like products for HCV, COVID-19, insulin or weight loss, the global revenues can be massive, and unjustified by the R&D costs, even when liberally adjusted for risks and capital costs or using reasonable hypothetical proxies for development costs.

For rare diseases there is a definite need to look at revenue milestones. Prices for cell and gene therapies are very high, and do seem extreme by anyone’s standards. To determine if a multimillion dollar gene or cell therapy price at the cost level of a new 3-bedroom home is justified, it is really necessary to look at the revenue milestones.

A few years back hospitals in Spain were providing CAR-T treatments for roughly 30 to 50 thousand euros, when the same treatments were priced at around \$350,000 to \$400,000 in the United States. The high U.S. prices are justified not only by the benefits of the treatments, often compared to other high priced interventions, but in the end, because people believe R&D is expensive and investors need incentives. But at some point the incentives are excessive.

We have encouraged policy makers to pay less attention to the prices of treatments for rare diseases and more attention to the revenue milestones. If a treatment is expensive now, and the patient population is small, it might be a reasonable incentive, regardless of who paid for the research. But when products for rare diseases generate billions in revenues, at some point prices need to come down, because the incentive has been paid for, in some cases, many times over.

We have recommended for some NIH-funded inventions licensed to third parties that after the first billion dollars in revenue, exclusivity be reduced by one year for every additional \$500 million in revenue, or steps be taken to progressively lower prices.

Access in developing countries

The United States has agreed at the World Health Organization (WHO) and the World Trade Organization that intellectual property laws should be implemented in a way to promote access to medicine for all. In fact, many if not most new NIH-funded biomedical inventions are shockingly unequal in terms of global access. This is particularly true for treatments for rare disease and cancer, and for the new cell and gene therapies.

For countries with a per capita income less than 30 percent of the United States, the U.S. should grant march-in requests when petitioned, if products are not available for most people that need them, in a developing country.

It's one thing if Pfizer or Novartis take actions that lead to inequality of access, but it's another if the restrictions on access are a direct result of monopolies of medical products invented through federal grants and research contracts.

Both the march-in and the Section 202/209 government use rights apply to subject inventions and their use worldwide. The march-in right is particularly important in cases where the federal government will play no role in financing the purchase of products.

Complex Patent Landscapes

KEI has an extensive comment on the issue of complex patent landscapes, and discusses to tools available to address non-Bayh-Dole patents on the context of a march-in case.

see: KEI Comment to NIST on Bayh-Dole Rights and Cases of Mixed Patent Landscapes. February 6, 2024. <https://www.keionline.org/39391>

Administrative and judicial appeals, injunctions and stays

Xtandi was registered with the FDA in 2012. In 2016, the first Xtandi march-in petition was filed and rejected by the Obama Administration. Another march-in effort was made in the Trump Administration, which was rejected in 2023, and HHS took until yesterday to uphold the NIH rejection of the petition.

In 2023 the NIH justified its rejection in part on the grounds that the appeal process would take too long, even though the patents run to 2027. HHS cited the same issue: the time it takes to go through the process including the appeals. (After dragging out the process for years).

The prostate cancer patients in the Xtandi case, asking since 2016 for the government to address the well documented pricing abuse, urged both the NIH and HHS to immediately use its Section 202 royalty-free license permit generics to enter the market now (FDA-approved generics are ready to enter the market when the patent issues are resolved) while the march-in process plays out. The Section 202 license is limited to use by or for the government, but since most of the market for Xtandi is from Medicare and Medicaid, this is very consequential. The Biden Administration could even use Section 1498 to ensure that no injunction was even possible, and at no cost since the Section 202 license means the compensation would be zero.¹

This is an illustration of how the government can deal with a barrier, if it actually is trying to lower drug prices. The guidance needs to explain these options too.

Disclosure: My older brother Clare Love is a Vietnam Vet, a prostate cancer patient, one of the petitioners, and one of the many persons impacted by the restrictive formulary for Xtandi.

Sincerely



James Love

¹ For more on using the Section 202/209 and Section 1498 rights in conjunction with march-in rights, see: KEI Comment to NIST on Bayh-Dole Rights and Cases of Mixed Patent Landscapes. February 6, 2024. <https://www.keionline.org/39391>

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ANNEX Pricing Clauses in U.S. Government Contracts for COVID-19 Products

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In 2020 and 2021, several U.S. government contracts for the development of COVID-19 vaccines, therapeutics, diagnostic tests and other related products included provisions on pricing. Some contracts include a most favored nation pricing clause that specifically requires the company to provide the U.S. government with “a price lower” than the price offered to any centralized federal authority that is “a member of the Group of Seven plus Switzerland.” The non-US members of the G7 are Canada, France, Germany, Italy, Japan, the United Kingdom.

Table A1, U.S. Government COVID-19 Contracts Containing Reference Price Constraints on Resultant Products

Contractor, Agency, and Contract Number	Subject	Page Located	Reference Price Term Excerpt
Most Favored Nation Clauses			
Eli Lilly The Army W911QY21D0012 P0002 April 7, 2021	Monoclonal Antibody Treatment Production	7-8	“H. 7 Sales to Covered Nations (i) Due to the exceptional and unprecedented nature of the COVID-19 threat to global public health, as well as the investments made towards the development of a safe and effective therapeutic against COVID-19, Lilly agrees that it will not at any time prior to 30 September 2021 sell any COVID-19 bamlanivimab/etesevimab combination

Contractor, Agency, and Contract Number	Subject	Page Located	Reference Price Term Excerpt
			therapeutic supplied directly to the Government under this Agreement to any centralized federal authority (i.e., federal government or equivalent) of a nation that is a member of the Group of Seven plus Switzerland ('Covered Nation') at a lower price than the prices set forth in this contract. . . ."
Eli Lilly The Army W911QY21C0016 October 26, 2020	Monoclonal Antibody Treatment Production	18	"H.7 Sales to Covered Nations (i) Due to the exceptional and unprecedented nature of the COVID-19 threat to global public health, as well as the investments made towards the development of a safe and effective therapeutic against COVID-19, Lilly agrees that it will not at any time prior to 30 June 2021 sell any COVID-19 therapeutic supplied directly to the Government under this Agreement to any centralized federal authority (i.e., federal government or equivalent) of a nation that is a member of the Group of Seven plus Switzerland ('Covered Nation') at a lower price than the prices set forth in this contract. . . ."
Merck Sharp & Dohme The Army W911QY21C0031 June 7, 2021	Therapeutic Development	21	H.7. Fully redacted including the title
Pfizer The Army W58P0522C0001 November 17, 2021	Paxlovid Purchase Agreement	33	H.7 Most Favored Nation Clause (a) If, at any time prior to, or during, the base term and any exercised options of this contract, Contractor enters into any agreement with a Covered Nation under which the Covered Nation commits to purchase (i) the same or a lesser volume of Product than the U.S. Government commits to purchase (ii) at a price lower than the price the U.S. Government is obligated to pay for Product under this contract, Contractor shall provide notice of such lower price to the U.S. Government within 30 days of the execution of the Contractor-Covered Nation agreement and the U.S. Government may elect, at its discretion, to receive the benefit of this provision and purchase the Product at that lower price.
Sanofi The Army W15QKN1691002; MCDC2011-005 July 30, 2020	Vaccine R&D and Production	28	"5.1 Most Favored Nation Clause (i) Due to the exceptional and unprecedented nature of the COVID-19 threat to global public health and in recognition of the long historical partnership between the U.S. Government and Sanofi Pasteur working on global pandemic solutions, as well as the investments made towards the development of a safe and effective vaccine against COVID-19, Sanofi Pasteur agrees that it will not sell any COVID-19 vaccine licensed under this Agreement to any nation that is a member of the Group of Seven plus Switzerland ('Covered Nation') at a price that is more favorable than those set forth in this Project Agreement."
Most Favored Customer Clauses			
ANP Technologies, Inc. The Army W911QY20D0019	Development and Production of a Diagnostic	11	"MOST FAVORED CUSTOMER H.1 Most Favored Customer

Contractor, Agency, and Contract Number	Subject	Page Located	Reference Price Term Excerpt
May 29, 2020			Awardee agrees that during the term of this contract and for a period of 5 years thereafter, that it shall not offer, sell or otherwise provide the production model of the CLIN 0001 end items (for the avoidance of doubt, CLIN 0001 end items in this clause shall mean a finished good of like material, like quality, to be used in a similar applications, and shall not include more general products to any entity at a price lower than that offered to the DoD. In the event that Awardee sells the production model at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the Contracting Officer in writing of the lower price. For prior purchases, the Awardee shall reimburse the DoD, the difference between the lower price sold to the other customer(s) and the price sold to the DoD multiplied by the number of items sold. Such reimbursement shall occur within thirty days (30) of the Awardee discovering that the lower price was given to another customer. Notwithstanding the foregoing, the Parties may agree to apply the difference in price paid by the other customer(s) and DoD into additional quantities required by the DoD."
AstraZeneca The Army W911QY2190001 October 9, 2020	Monoclonal Antibody Treatment R&D and Production	32	ARTICLE 9. Most Favored Customer A. In the event that the Parties agree to a follow-on production pursuant to 10 U.S.C. § 2371b, Awardee agrees that it shall sell to the U.S. Government the first million doses of AZD7442 at a price of [REDACTED]. Any additional doses will be sold to the U.S. Government at a price to be negotiated and agreed by the Parties. B. If Awardee develops a like product (commercialized version or derivative of the production model of the Prototype) with similar capability and intended application, but at a lower unit price ("Like Product") regardless of quantity, Awardee shall make the U.S. Government aware of that similar product and the technical and price differences between that product and the Prototype. Such notification shall be made to the OTA0 in writing, of which email is an acceptable form, within [REDACTED] of such offering.
Emergent BioSolutions Canada Inc. The Army W911QY2090013 June 24, 2020	Post-exposure Prophylaxis (PEP) Development	16	"ARTICLE 9. Most Favored Customer A. Awardee agrees that it shall not offer, sell, or otherwise provide the production model of the Prototype to any entity at a price lower than it offered to the DoD. In the event that Awardee sells the production model of the Prototype at a lower unit price than that price sold to the DoD, Awardee shall reimburse the DoD, the difference between the lower price sold to the other customer (S) and the price sold to the DoD multiplied by the number of items sold"
Immunome, Inc. The Army W911QY2090019 July 3, 2020	"research and development of a standardizable and scalable [REDACTED] comprised of [REDACTED] antibodies [REDACTED]"	16	"ARTICLE 9. Most Favored Customer A. Awardee agrees that it shall not offer, sell or otherwise provide the production model of the Prototype to any entity at a lower price than that offered to the DoD. In the event that Awardee sells the production model of the Prototype at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the OTA0 in writing of the lower price. . . ."
Inovio Pharmaceuticals, Inc. The Army	Vaccine Delivery Device Development	17	"ARTICLE 9. Most Favored Customer A. For a period of six (6) years from the Effective Date, Awardee agrees that it shall not offer, sell or otherwise

Contractor, Agency, and Contract Number	Subject	Page Located	Reference Price Term Excerpt
W911QY2090016 June 22, 2020			provide the production model of the Prototype to any entity at a price lower than that offered to the DoD. In the event that Awardee sells the production model of the Prototype at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the OTAO in writing of the lower price. . . .”
Maxim Biomedical, Inc. The Army W911QY20D0018 May 11, 2020	Diagnostic Production	10	“H.1 Most Favored Customer A. Awardee agrees that during the term of this contract and for a period of 5 years thereafter, that it shall not offer, sell or otherwise provide the production model of the CLIN 0001 end items (for the avoidance of doubt, CLIN 0001 end items in this clause shall mean a finished good of like material, like quality, to be used in a similar applications, and shall not include more general products to any entity at a price lower than that offered to the DoD. In the event that Awardee sells the production model at a lower unit price than that price sold to the DoD, Awardee shall immediately notify the Contracting Officer in writing of the lower price. . . .”
Murtech, Inc. The Army W911QY20D0017 May 11, 2020	Diagnostic Production	15	“H.1 Most Favored Customer A. Awardee agrees that during the term of this contract and for a period of 2 years thereafter, it shall not offer, sell or otherwise provide the production model of the CLIN 0001 end items (herein the ‘Items’) (for the avoidance of doubt, CLIN 0001 production model end items in this clause shall mean a finished good of like material, like quality, to be used in a similar applications, and shall not include more general products) to any entity at a price lower than that offered to the DoD.”
Novavax The Army W911QY20C0077 P0002 June 4, 2020	Vaccine Development and Production	4	“The Contractor shall maintain a most favored customer provision for the product once authorized or licensed by the FDA, such that the Contractor shall not give any entity a better price than the DoD for a period of five (5) years from the award of this contract, limited to customers in the U.S. and purchases made in the U.S to include sale prices as compared to commercial clients with respect to quantity, location of delivery, fundamental differences in deliverable formulation, and material differences in terms and conditions for commercial contracts.”
Rigel Pharmaceuticals The Army W911QY2190018 January 29, 2021	Therapeutic Development	29	ARTICLE 20. Most Favored Customer. A. In the event that the Parties agree to a follow-on production agreement pursuant to 10 U.S.C. 2371b, Awardee agrees that it shall sell to the U.S. Government up to [REDACTED] treatment courses of TAVALISSE at a price not greater than [REDACTED]. Any additional treatment course will be sold to the U.S. Government at a price to be negotiated and agreed by the Parties. B. If Awardee develops a like product (commercialized version or derivative of the production model of the Prototype) with similar capability and intended application, but at a lower unit price (“Like Product”) regardless of quantity, Awardee shall make the DoD aware of that similar product and the technical and price differences between that product and the Prototype. Such notification shall be made to the OTAO in writing, of which email is an acceptable form, within thirty (30) days of such offering.

Contractor, Agency, and Contract Number	Subject	Page Located	Reference Price Term Excerpt
60 Degrees Pharmaceuticals The Army W911QY2190011 December 4, 2020	Therapeutic Development	16	Article 9. Most Favored Customer A. [REDACTED] [REDACTED] C. This Article applies only to products sold in the [REDACTED] related to COVID-19.
Government Preference Clauses			
Becton, Dickson & Company The Army W911SR2030001 July 1, 2020	Needle Production	17	“9. Government Preference 9.1 Pricing. During the term of the Agreement, the Recipient agrees that, in the event that it enters into a Group Purchasing Organization (GPO) contract with a Qualifying Third Party (as defined below) with respect to a Qualifying Product (as defined below) with a per unit GPO price lower than that offered for the same Qualifying Product to the Government, the Recipient shall (i) promptly notify the Agreements Officer in writing of the lower price and (ii) extend the lower price to all future sales of the Qualifying Product to the Government. . . . “ For purposes of this section, “Covered Nation” shall mean a nation that is a member of the Group of Seven (Canada, France, Germany, Italy, Japan, the United Kingdom, and the United States) plus Switzerland.
Global Life Sciences Solutions The Army W911NF2130001 October 13, 2020	Expanded Manufacturing and Production Capacity	8	9. Government Preference 9.1 [REDACTED] 9.2 [REDACTED] 9.3 [REDACTED]
Retractable Technologies, Inc. HHS W911SR2030004 July 1, 2020	Expansion of Manufacturing Capacity of Needles/Syringes	23	9. Government Preference [REDACTED]
SIO2 Medical Products, Inc. The Army W911NF2030003 June 5, 2020	Vaccine Delivery Device R&D	13	“9. Government Preference 9.1 Pricing. During the period of performance and the exercised optional availability periods, the Recipient agrees that, in the event that it offers, sells or otherwise provides a Qualifying Product (as defined below) to any Qualifying Third Party (as defined below) at a per unit price lower than that offered for the same Qualifying Product to the Government or a third party purchasing Qualifying Product pursuant to a designation by the Government pursuant to Section 9.2 or 9.3 (an ‘MCM Partner’), the Recipient shall (i) promptly notify the Agreements Officer in writing of the lower price and (ii) extend the lower price to all future sales of the Qualifying Product to the Government or an MCM Partner.”

