Brigham and Women's Hospital
Founding Member, Mass General Brigham

HARVARD MEDICAL SCHOOL

MULTI-REGIONAL CLINICAL TRIALS
THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

Submitted July 22, 2024

Re: **NOT-OD-24-125**
NIH-OSP Draft NIH Intramural Research Program Policy: Promoting Equity Through Access Planning

To whom it may concern:

The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard ("MRCT Center") appreciates the opportunity to comment on the Draft Policy by the National Institutes of Health Office of Science Policy (NIH-OSP) entitled, "*Intramural Research Program Policy: Promoting Equity Through Access Planning*," published at 89 Fed. Reg. 45003-05 (May 22, 2024) (the "Draft Policy").

The MRCT Center is a research and policy center that seeks to improve the ethics, conduct, oversight, and regulatory environment of international, multi-site clinical trials. Founded in 2009, it functions as an independent convener to engage diverse stakeholders from industry, academia, patients and patient advocacy groups, non-profit organizations, and national drug and device regulatory agencies. The MRCT Center focuses on pre-competitive issues, to identify challenges and to deliver ethical, actionable, and practical solutions for the global clinical trials enterprise. The responsibility for the content of this document rests with the leadership of the MRCT Center, not with its collaborators nor with the institutions with which its authors are affiliated.[1]

The MRCT Center applauds NIH-OSP's efforts to promote greater access—and equitable access—to therapeutic interventions derived from taxpayer dollars invested in research performed by investigators at the IRP. We offer the comments below to further NIH-OSP's efforts.

Comments

1. Promoting meaningful access approaches.

NIH intends to provide additional guidance to licensees on examples of acceptable, commercially reasonable approaches for promoting access. NIH is seeking input on the range of activities that could be considered and strategies to mitigate access challenges and expand the reach, and benefit, of drugs, biologics, vaccines, and devices stemming from NIH inventions.

In the Appendix of the Draft Policy, NIH-OSP lists several examples for how licensees might promote equitable access. These include "committing to keep prices in the U.S. equal to those in

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other developed countries; not raising costs above inflation; preparing tailored, culturally sensitive educational materials for a range of domestic and global patient populations." 89 Fed. Reg. 45005. We worry that the presentation of the development of educational materials as tantamount or equivalent to price controls in this context may affect the success of the Draft Policy's goal to promote equity through access planning. Licensees are unlikely to subject themselves to price controls voluntarily: we strongly recommend differentiating proposed price control mechanisms for licensees from other aspects of access planning. NIH-OSP is likely to meet resistance from licensees from private enterprise when suggesting price controls in any case, but NIH-OSP could amend the Draft Policy to require both a price control element to address "persons…adversely affected by persistent poverty of inequality" and an educational element to address cultural barriers.

2. Promoting transparency in the biomedical enterprise and return on investment.

NIH The process of bringing a new product through research and development, to market, and into the hands of patients is long, fraught with challenges, and expensive. NIH is interested in hearing from potential partners on how access plans could incorporate transparent cost accounting measures to assist NIH in driving down costs associated with innovation and making clearer what costs are incurred along the way and how those affect product costs.

The actual manufacturing and development costs, fully burdened with overhead and sunk costs, are are at best inexact estimates; such a proposal would be met with strong resistance and could be misinterpreted by the public. Even the economics of the basic science to potential product license within the IRP is hard to estimate: does one include the years of misdirection and failed experiments? And in the IRP, the NIH has a firm handle on the accounts. Generally, pharmaceutical manufacturing achieves economies of scale during the lifecycle of a drug, biologic, vaccine, or device patent, but the investment is greater earlier than later—how would that factor into the access plan? Would the public (and Congress) then anticipate that "transparent cost accounting measures" are auditable? And any such estimate is subject to misinterpretation: the published cost accounting for the development of NIH-licensed Drug A through manufacturing might be mistaken for the unpublished development cost of non-licensed Drug B.

To help avoid potentially fractious drug pricing discussions that radiate out beyond NIH's book of licensed products, NIH may want to reevaluate how transparency in development costs meets the objectives laid out in NIH's definition of "access" – product affordability, availability, acceptability, and sustainability. In our opinion, none of these characteristics is based on the costs of development and manufacturing, but rather the need to provide access to essential products.

We offer an alternative approach. For those products developed with public funds invested in the research of the IRP, some percentage of total revenue should be invested back into the public good. This cannot be presented as a 'tax' but rather, essentially, a form of a royalty stream. That

percentage could be variable based on time on the market or other factor, but it will reflect the success and impact of the product. Those funds could be ear-marked to the NIH, HHS, the very patient populations who cannot afford the product, or other specified purpose (e.g., insurance for participant injury as a result of participation in investigational clinical research). This model has certain advantages: it is easy to calculate, the funds transfer is visible and directed to the public good, and the pharma industry is accustomed to this model in that licensing and royalty streams are common in academic centers that license their discoveries. Note that the percentage of revenue (rather than "net profit" which again is a financial calculation that can be modified depending on numerable factors and is very difficult to audit) need not be large to have a substantial financial impact (e.g., 1% of a $1B product is $10M year over year).

3. Providing flexibility while achieving clear policy objectives.

NIH recognizes that its licensees, their partners, and the public will need confidence around what this policy requires and the standards that would be used to evaluate plans. The agency is seeking input on how to maintain flexibility for licensees to pursue their specific product development and commercialization needs while simultaneously promoting certainty and transparency on access efforts and policy enforcement.

The Draft Policy appears to take into account the wide range of development costs incurred from drug to drug and from medical device to medical device. However, the Draft policy's differentiation between "late-stage" and "early-stage" inventions seems incomplete. Because so few early-stage inventions eventually to reach the market, NIH-OSP should consider a boilerplate option for licensees that is balanced by the stage of discovery. For instance, given the model proposed above (percentage of revenue), the specific percentage may be less if early-stage and somewhat greater if later stage. This simplicity also has other advantages: the opportunity costs of developing access plans are minimized when considered against bespoke access plans for each of NIH's licensed assets. We would suggest NIH-OSP develop a single (but flexible) framework to apply to all assets, determined at licensing or another date certain (e.g., when the asset reaches a first pivotal trial) and reviewed every 5-8 years to assess workability and impact.

4. Helping licensees achieve access goals.

NIH is interested in hearing ideas about how it may be able to help licensees deliver patient access to products that stem from these agreements. Licensees could include such information in access plans or at earlier stages of product development. NIH invites input on additional steps it could take or ways to leverage existing U.S. government programs and resources to assist in this endeavor.

Each licensee is likely to have different strengths and weaknesses when it comes to promoting equity access. For example, a global pharmaceutical company would be considerably more likely to have the capability to bring a drug to populations in low- and middle-income countries – see

appendix at 89 Fed Reg 45005 – than would a start-up or a small biotech firm. With that in mind, the entire group of licensees across NIH's portfolio are likely to require a wide array of support to help promote patient access for their individual licensed products. Therefore, we suggest that organizations seeking NIH licenses be evaluated or submit self-evaluations to identify the patient access strengths and shortcomings in their capabilities. Simply put, the best way NIH could help licensees deliver patient access is to know what they need. These needs would be best assessed at the "early-stage" of the tiered approach described in the Draft Policy (if that tiered approach is retained in the final policy) to give both the licensee and NIH sufficient time to respond to whatever the need may be.

5. Establishing licensee obligations depending on the stage of technology development.

Generally, as a product moves closer to market, the odds of successful commercialization improve, and NIH's proposed policy would take this into account. If the agency has advanced products to the point of a first pivotal clinical trial (e.g., Phase III or the equivalent)—licenses covering those products would include specific, tailored access-oriented provisions that should be clear and understandable. NIH is seeking further input on specific provisions that would meet these objectives.

We fully support the early-stage and late-stage distinction between requirements for licensed products. NIH-OSP should consider developing specific guidance for each of the options provided in the bulleted list in Part III of the Draft Policy's appendix at 89 Fed Reg 45005. For some licensed products – e.g., vaccines or next-generation antibiotics – partnering with public health organizations may make sense, while for other licensed products – e.g., a medical device implant – it may not. Consequently, NIH-OSP should develop guidance or a checklist for licensees to help them distinguish how best to promote patient access impactfully.

Furthermore, the MRCT Center has long been a proponent of "clear and understandable" language to promote health literacy.[2] Access plans should always keep the intended patient population in mind throughout their development from early-stage to late-stage to marketed products. The access plans should be culturally and linguistically appropriate for the populations intended to benefit.

Lastly, we suggest that NIH-OSP consider flexibility as to the stage of development when access plans would be required. For example, phase IIb trials as a time when, at least for a number of products (e.g., oncology), the potential product has been derisked significantly. Device development often proceeds at a different pace. The timing should be conditioned on the product.

[2] Especially if the licensee intends to develop educational materials to promote tailored access, suggest leveraging the MRCT Center's health literacy resources and plain language glossary, the latter of which has already been indexed by NIH and adopted as a global standard by the Clinical Data Interchange Standards Consortium (CDISC).

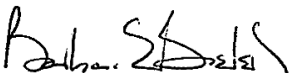
6. Assessing policy impact.

NIH is seeking input on how to assess compliance with the proposed policy and potential metrics for assessing its impact.

Because the Draft Policy applies to products in development, it appears the best to measure the policy's impact would be two-fold. First, independent, multi-stakeholder reviewers could assess the strength or completeness of access plans to measure uptake and incorporation of the Draft Policy's goals and ideals among licensees. Second, once a licensed product reaches the market, direct engagement with community stakeholders and patient advocacy groups by NIH may be an important way to evaluate which elements of a particular product's access plan deliver value to communities and patients. NIH should consider formalizing internal infrastructure to perform this function as part of its own access by design planning.

As mentioned above, the MRCT Center supports NIH-OSP's efforts to equity through access planning. The MRCT Center appreciates the opportunity to comment on this Draft Policy. We would welcome an opportunity to discuss. Please feel free to contact the MRCT Center or me (bbierer@bwh.harvard.edu), if we can be helpful.

Respectfully submitted,



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