Re: National Institutes of Health (NIH) Office of Science Policy (OSP): Request for Information on Draft NIH Intramural Research Program Policy: Promoting Equity Through Access Planning

July 22, 2024

Attn: National Institutes of Health, Office of Science Policy

Re: 89 RF 45003

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To Abby Rives and whom else it may concern,

The Innovative Genomics Institute (IGI), a public, academic research institute formed in partnership between multiple University of California campuses, and the Global Gene Therapy Initiative, a global community of clinicians, researchers, and advocates advancing cell and gene therapy access around the world, below submit comments to the request for information on the Draft NIH Intramural Research Program Policy to Promote Equity Through Access Planning.

To provide the Agency with a spectrum of views on how to best approach access planning, we relied on our joint network of experts and practitioners. Rather than working to achieve consensus among these contributors, we are presenting a catalogue of ideas and options that the NIH may wish to consider as it finalizes this important policy and develops its implementation. We note that, therefore, the content of this letter may not fully reflect the views of any one of our contributors. Given the IGI's and GGTI's research priorities, some ideas may be best suited for innovative cell and gene therapies. However, we sought to provide recommendations that can be applied broadly to IRP inventions.

We thank the NIH Office of Science Policy for advancing this critical policy. As practitioners in the innovation space we are encouraged that the largest public funder of research is committing to improving access to health innovations *for all*. So often have arguments of threats to innovation and investor appetite have meant that American taxpayers must contend with inadequate and inequitable access to the innovations developed with those funds. We recognize that the US healthcare system is complex and that, at times, innovation and access are in tension with each other. Nonetheless, it is crucial that taxpayers reap the benefits of their investments in biomedical education, research, and development. Our organizations welcome any questions or the opportunity to provide further information as needed.

On behalf of the Innovative Genomics Institute and the Global Gene Therapy Initiative,

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General Comments on the Draft Policy

This policy is an important step, but expansion of these requirements to extramural research is imperative. We applaud this step by the NIH to promote equitable access; however, recognizing that some industry licensees may be less inclined to license IP from the NIH as a result, several experts recommend expanding these requirements to all IP generated using NIH/government funding. Such a sweeping policy change would make access planning the new norm and help stakeholders identify the types of provisions that most effectively improve access in various contexts. We believe that many foundations and philanthropic donors would follow suit as well. Naturally, such a step would require dedicated resources. Centralized consortia of experts in licensing could help streamline this work for institutions that may not have the resources to staff their technology transfer offices appropriately.

The NIH should hire mission-driven staff with deep industry understanding and strong negotiation skills. Implementation of this policy will come with unique challenges; expert staff should be given the time and flexibility to navigate and respond to these challenges, rather than NIH reversing course. In addition, NIH should work with ARPA-H who has also expressed interest in promoting equity in their commercialization plans (see also, **Interagency Collaboration**). We encourage the Agency to be transparent with stakeholders about these challenges and lean on the community to overcome them. NIH staff tasked with policy implementation should also be empowered to work with the Office of Science Policy to advance the expansion of access planning policies beyond the intramural research program.

Requiring an Access Plan at the pivotal trial stage is too late. Licensees should think about affordability, availability, acceptability, and sustainability from an earlier stage in development. Several experts recommend moving this requirement to the time enrollment for clinical trials is initiated (Phase I). For example, a vaccine product against a tropical disease that has to be stored at -80°C will likely only reach patients in higher-resource settings and not the majority of patients in the countries where the disease is endemic. Such considerations should have to be made prior to the establishment of commercial manufacturing processes.

The Access Plan should cover *both* underserved US populations and patients in low- and middle-income countries (LMICs). The model agreement language in its current form opens the door for licensees to provide a plan that benefits *either* LMICs or underserved US populations. Unless the specific IP is only applicable to one of these populations (a determination that NIH should make on a case-by-case basis only upon written request by the licensee), the policy should not allow licensees to do the bare minimum in just one population in order to check a box. Additionally, licensees should outline how their plans address availability, acceptability, affordability, and sustainability. For example, donation of 10,000 diagnostic kits for an infectious disease does not meaningfully tackle the sustainability pillar.

Licensing language should be tailored to different types of cases. Due to the diversity of IP, the stage of licensing, and its uses, we suggest that NIH develops multiple iterations of the model language for different cases. We recommend considerations of whether the IP is intended for a global health (security) application; whether the license is exclusive or non-exclusive; and to take into account whether the IP was licensed at an early or late stage of development. Specifically for IP that is licensed at an early

stage and where NIH IP comprises only a small portion of the final product, NIH could incentivize licensees to engage in access planning, but it may be unreasonable to ask licensees to commit to expansive access provisions. On the other hand, where NIH has de-risked a product substantially, licensing language should clearly outline expectations of access plans and robust enforcement mechanisms.

Expanding the list of underserved populations in the United States. The model language should explicitly discuss promoting access for un- and underinsured populations and incarcerated persons.

Activities to promote equitable access

Upon convening a yearlong, multi-disciplinary task force of experts and practitioners in the space, the Innovative Genomics Institute last year produced an extensive report on making genetic therapies more affordable and accessible. Some deliberations focused specifically on access provisions in licensing agreements. Below we include some recommendations from the task force as well as additional activities proposed by contributors we interviewed:

- **Instituting a "most-favored" nation clause that would prevent US patients from paying more than patients in economic peer countries.** The American taxpayer, on average, pays 4.22 times more for brand-name prescription drugs than taxpayers in peer countries such as Japan, Germany, France, and the United Kingdom. In addition, they will often have paid for the discovery research and early development of the drug product, and then are asked to pay again in the forms of social security tax and insurance premiums (and co-pays should they themselves need the product) for already inflated drug prices compared to other high-income countries. The passage of the 2022 Inflation Reduction Act and its price negotiation scheme is a noteworthy step in this direction.

- **Including provisions for price reductions once preset sales volumes are reached.** Alternatively, royalty payments could be substantially increased in the absence of such reductions in price.

- **Granting voluntary, non-exclusive licenses directly to third parties, such as the Medicines Patent Pool (MPP)**, and working with organizations with established delivery networks to achieve access goals. Gilead and Bristol-Myers Squibb have taken such approaches for their Hepatitis C drugs, for example, with improvements in access as a result.

- **Licensees could work with community groups, clinics, and federally qualified health centers (in the US) to understand barriers to access** and inform an effective access plan. This would be particularly impactful if done early during the design phase of commercial products.

- **Developing detailed commercialization plans for LMICs**, including plans to engage local regulators and payors. Ideally, these plans would be drawn up alongside design considerations and prioritize sustainable access. As discussed above, access plans should benefit both US populations and patients in LMICs; LMIC commercialization plans could therefore be made mandatory unless there is reasonable cause to grant an exemption of a product for deployment in LMICs.

- **Entering into manufacturing or purchasing partnerships with mission-oriented organizations.** Manufacturing can have tremendous implications for access and price. In the US, a pharmaceutical company could, for example, partner with a public or nonprofit institution, such as the CalRx program in California, to manufacture a portion of its product which is then sold to the state's Medicaid population at a discount or on a cost-plus basis. In LMICs, manufacturing hubs and/or decentralized manufacturing facilities could be established that enable technology transfer.

- **The NIH, in collaboration with the FDA, could establish a network of manufacturing entities in LMICs** that have the capability to manufacture drug products. Licensees could be directed towards working with these entities to produce and market, or out-license drugs on a cost-plus basis for LMICs. These products could have specific markings or labels so they do not end up in high-income markets. Developing in-country infrastructure would, among other benefits, reduce manufacturing costs and increase the volume of product on the market. US manufacturers could still make a profit, albeit smaller, while improving patient access.

- **For IP where NIH sees outsize benefits for underserved populations or for global health security, the Agency could seek to establish multi-party cooperations of mission-aligned collaborators for licensing and development of the final product.** These collaborations could be incentivized, for example by reducing royalty payments or providing additional research grants for academic contributors. Such multi-party alliances can lower overall development costs, promote transparency, and enhance downstream access. (For a deeper discussion of this topic, see Mimura et al., *Perspective: Socially Responsible Licensing, Euclidian Innovation, and the Valley of Death,* Stanford Journal of Law, Science and Policy, 2011.)

- **For entities that are unable to fulfill their access provisions, NIH may consider levying a penalty of a pre-negotiated percentage of sales to be paid into an access fund** which the Agency then leverages to support equitable access initiatives (e.g., procurement programs for low-income individuals) and research in relevant areas. The percentage could be set in tiers based the extent to which the final product is comprised of NIH IP, the degree to which NIH de-risked the product, and how much taxpayer funding went into the final product.

Incentives and Enforcement

Since commercial entities are likely to view access planning policies as cumbersome requirements and may consider avoiding NIH-owned IP altogether (see also, **General Comments**), many of our contributors pointed out the importance of incentive structures that will encourage licensees to come to the table and negotiate access plans that have meaningful impacts in underserved US and LMIC populations. Importantly, robust incentives may convince licensees of early-stage IP where taxpayer funding did not substantially contribute to the final product to submit an ambitious Access Plan.

The NIH could convene stakeholders to understand how data packages could be made more 'commercial ready' during early development to streamline downstream processes for future licensees. For example,

data packages already prepared in the eCTD format that FDA expects for data submissions could reduce the administrative burden on licensees. The NIH (or partners like the FNIH) could also cultivate a list of organizations committed to healthcare access across diverse populations with whom licensees could work to implement their access plans.

While incentives are critical, the NIH policy should also be clear about enforcement mechanisms of an Access Plan. This is particularly important for largely de-risked, late-stage products and exclusive licenses. For exclusive licenses, failure to comply with access provisions could result in conversion of the license to a non-exclusive license and potentially automatic sharing with Medicines Patent Pool (MPP) or another organization with the ability and intent to provide the product to underserved populations. Tax penalties or increased royalty payments could also be levied for non-compliance. Where political will is lacking for such enforcement mechanisms, the NIH could collaborate with other countries, such as Japan, Germany, or the United Kingdom, who have prioritized patient access in the past and may be more willing to leverage their market size to require companies to comply with access provisions for LMICs. Revocation of a license should be seen as a last resort, but nonetheless employed when a licensee does not meet agreed upon access provisions.

Transparency and pricing

There is considerable diversity of thought in the field regarding transparency measures. Some have suggested that cost transparency is essential in order to enhance affordability and access, especially for cost-plus pricing. Others have expressed that transparency around the cost of goods and labor is uninformative, and that transparency measures should focus on the cost of development, including the cost of capital and failures in the pipeline. Others again have suggested that, since pricing of a drug or technology may be set based on unrelated business considerations, transparency should focus on profit margins instead and royalties to the licensor set in relation to profits. Lastly, it has also been suggested that cost transparency may not be relevant if a licensee is able to meet meaningful access milestones.

An alternative to transparency measures that was proposed is a multi-stakeholder price review panel that includes representatives from FDA, CMS, experts in the field, and citizens (i.e., taxpayers). Such a panel could review data on the safety, efficacy, and cost effectiveness of a drug (as is done in much of the world as part of a health technology assessment process) and help determine appropriate prices based on the amount of public funding that contributed to the development of the final product. This approach may be particularly suitable for products that were largely de-risked by the NIH and licensed at a late-stage. (We note that if this policy were expanded to extramural research, cell and gene therapies could be made substantially more affordable and accessible by such a measure. A majority of all cell and gene therapies are developed and advanced through early clinical trials by government-funded academic institutions. These transformational products can have multimillion dollar price tags that are determined solely by the commercial entity that obtained marketing approval for the final product, without regard for the amount of taxpayer money that funded discovery, preclinical, and early clinical work.)

Interagency Collaboration

A number of steps with farther reaching implications could be taken if the government were to take a more concerted effort to improving equitable access. Especially agencies within the Department of Health

and Human Services could coordinate efforts and pilot new models. Contributors discussed, for example, that ARPA-H has also expressed interest in identifying novel contracting and commercialization strategies that ensure access to the health innovations it funds for all. ARPA-H is well positioned to experiment with new methods and bring together government stakeholders and commercial entities.

HHS agencies could also collaborate on creating interagency incentive structures that reward access milestones. For example, NIH could reduce royalties from discounted sales (for underserved US populations) or sales in LMICs, FDA could establish a priority review voucher program, or CMS could guarantee exclusion of a drug that has been made accessible in underserved populations from future price negotiations under the Inflation Reduction Act. The federal government (or state governments where access provisions have an outsize impact) could also provide tax breaks to licensees who are particularly successful in the implementation of their access plan. The NIH could also work together with the Centers for Medicare and Medicaid Services (CMS) to tie coverage and reimbursement of a product in the US to license sharing with MPP or a similar organization.

We note that many of these efforts will require an act of Congress or additional regulatory authority. However, with recent use of a most-favored nation clause and the passage of the Inflation Reduction Act (in some ways asking CMS to act as a health technology assessor), there appears to be appetite among lawmakers to trial such changes that could reduce the cost of prescription drugs and healthcare to patients and the system.

Conclusion

The American taxpayer invests substantial amounts of money into research and development with the expectation that returns on this investment will be reaped with respect to their health and healthcare. Instead, Americans have poorer health outcomes, lower life expectancy, and higher healthcare and prescription drug costs than citizens of equally wealthy nations. Support for innovation and a thriving business ecosystem should not come at the expense of the very people who supported innovation. We are therefore encouraged by NIH's Intramural Research Program championing a new approach to licensing practices in the public sphere. As outlined, we encourage NIH to be bold in their approach, work with its governmental and non-governmental partners in implementing successful strategies to equitable access, and swiftly expand its vision for access beyond the walls of the Institutes.

We look forward to learning more about the implementation of this policy and welcome opportunities to engage further in the future.

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Please note that some contributors chose not to be attributed here as this was not developed as a consensus document.