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

Thank you for the opportunity to comment on the updated draft NIH intramural research program policy. We are members of the Yale Collaboration for Regulatory Rigor, Integrity, and Transparency (CRRIT), an interdisciplinary initiative aligning research on medical product evaluation, approval, and coverage with the goal of advancing policies that improve patient outcomes. On behalf of CRRIT, we laud NIH for its efforts to ensure that federally funded advances in biomedical research are available and affordable. We agree with many aspects of the updated guidance, particularly that access plans will be required to “[detail] steps they intend to take to promote patient access to those products.” However, we believe that more can be done to ensure the affordability and accessibility of taxpayer-funded health technologies, both in the United States and in low- and middle-income countries (LMICs).

In our comments below, we offer suggestions to strengthen guidance on the content, implementation, and oversight of proposed access plans.

Recommendations

Access plan characteristics

1. **Scope:** What technologies should be covered, and which populations should be included in access plans?
 - 1.1. **Change “and/or” to “and”:** The draft “Policy Requirements” currently suggest that access plans should apply to underserved U.S. populations “and/or” populations in LMICs. Fulfilling NIH’s aim to “drive effective partnerships that foster a shared commitment to transforming knowledge into improved health for all” demands that this be replaced with “and”.
 - 1.2 **Expand covered technologies:** The policy applies to patent licenses for the commercialization of “drugs, biologics, vaccines, or devices.” This should be

expanded to also include diagnostics, as well as a more open-ended “and other technologies and/or procedures with medical use”. The U.S. is unusual globally in deeming some abstract ideas patentable, for example surgical and diagnostic procedures (1,2). Without this amendment, the guidance risks inadvertently excluding products within the scope of the overall intent, for example digital technologies, artificial intelligence products, and medical treatment processes.

2. **Improving the clarity and rigor of the guidance**

2.1 **Providing context-specific guidance to improve the quality of access plans:**

NIH has proposed “provid[ing] additional guidance to licensees on examples of acceptable, commercially reasonable approaches for promoting access”. NIH should provide model licenses and access plans for several types of technologies and market contexts. Licensees should have flexibility that accounts for product diversity in developing access plans, but case examples would support NIH in communicating the minimum standards expected in access plans. Other licensing entities, including universities, have published such model licenses and access plans on their technology transfer websites, thus providing anticipatory guidance to potential licensees on what the minimum terms would include (3,4).

2.2 **Starting early to lay groundwork for access plans:** Publicly supported research can result in greater returns if planning for access begins well before licensing of these inventions takes place. Moreover, earlier consideration around access plans could also assist NIH in anticipating how a NIH-licensed invention as a component of a commercialized product might be strategically best managed to ensure the twin public interest goals of innovation and access to those in need. Discussions with potential access partners, licensing with WHO’s Health Technology Access Pool (HTAP), the proposed NIH Access Advisory Council, and key academic and civil society experts can inform and give contour to more effective access plans down the road.

3. **Minimum standards:** NIH should provide clarity in the guidance about the minimum standards (i.e., a “floor”) that partners should be expected to start from in developing their access plans. Our comments are structured around NIH’s proposed “factors affect[ing] access”.

3.1 **Affordability:** We applaud the guidance for recognizing a range of strategies to optimize affordability and access within the constraints of sustainability. However, more specific measures should be included in the guidelines to support licensees (and NIH monitoring and evaluation) in assessing whether products are affordable.

3.1.1. **Cost of goods sold (COGS) and market analysis:** Although COGS analysis is foundational to many elements in the proposed guidance, the draft guidance does not specifically require that it be provided to NIH. Licensees should provide independent COGS analysis and market analysis to estimate the marginal cost of production at different

production volumes and the estimated market size at different price points. COGS analysis is standard practice in Federal Acquisition Regulation (FAR, see 15.404-1) and the Defense Acquisition University (DAU) Cost Analysis Contract Pricing Reference Guide (5,6). There will be inflection points associated with economies of scale, and such analysis can help inform what market size would be necessary to achieve cost reductions. We support provisions in the guidance proposing that stock be sold to designated entities on a cost-plus basis.

- 3.1.2. **Other cost inputs and expenditure forecasting:** Licensees should provide documentation with disaggregated past and expected future costs (e.g., R&D including pre-clinical study and clinical trial costs, regulatory costs, and marketing costs) of the product(s) to which the NIH licensed invention might contribute. This information is essential in assessing the overall return on investment (ROI) and fair prices. This will also assist NIH in determining the true impact of public investment on various public health and economic measures (7).
- 3.1.3. **Measures of affordability:** At minimum, licensees should commit to international reference pricing (i.e., prices in the U.S. should not be higher than any country within a set comparator group of countries) to set U.S. prices for any health technologies yielded from licensed intramural research program patents. Licensees should commit to collecting data on end-user costs (i.e., costs to users by insurance type, including among uninsured people). As appropriate, licensees should propose access plans to provide access to particularly low-income or otherwise vulnerable patients. R&D costs should be recouped in high-income countries and not in low- and middle-income country markets to the greatest extent possible. To optimize access, low- and middle-income country pricing should be informed, as much as practicable, by marginal production costs. NIH could also consider other established measures of affordability for low- and middle-income countries, including the World Health Organization (WHO) and Health Action International (HAI) pricing index, which compares the price of a drug in relation to the wages of the lowest paid, unskilled government worker within the country and assesses the number of days such a person would have to work to afford the drug (8).
- 3.1.4 **Abusive pricing protections:** A profit ceiling should be imposed (taking into account R&D including public contributions, manufacturing, marketing, and other operational costs), after which excess profits are subjected to higher royalty rates and/or taxes (9). The COGS analysis can provide a starting point for assessing fair returns, both for the licensee and for taxpayers from the NIH contribution.

3.2 Availability and sustainability

- 3.2.1. **Market exit:** Licensees should provide advanced notification (18 months, as recommended by WHO) of any anticipated product discontinuations and/or withdrawals from specific markets (10).
- 3.2.2. **Ensuring supply continuity:** Access plans should include provisions that should the licensee leave the market, they must commit to sublicense to and provide technology transfer to another manufacturer (with access provisions carried over), or else permit NIH to retain intellectual property and know-how, and issue non-exclusive licenses to other manufacturers to ensure sustainable supply.
- 3.2.3. **Third party licensing partners:** The guidance currently includes licensing to public health patent pools. While we do not oppose the inclusion of the Medicines Patent Pool (MPP), the WHO Health Technology Access Pool (HTAP) should be the patent pool of first resort. Although we have great admiration for the work of the MPP, HTAP is an intergovernmental agency with enhanced capabilities compared to the MPP to support product development and uptake (e.g. incorporation into disease treatment guidelines, supporting prequalification for procurement, ensuring regulatory harmonization, and building partnerships with product development partnerships). MPP licenses have also frequently excluded many LMICs, which would not be in line with NIH's commitment to promote access across LMICs.

3.3 Acceptability

- 3.3.1. **Adaptation:** Access plans should require licensees to conduct further studies to understand barriers and drivers to adoption in target populations, with particular attention to underserved U.S. and low- and middle-income country populations. If such studies are not feasible, NIH should be permitted to conduct such studies or allow third parties including other federal agencies to do so, with licensees providing any intellectual property, clinical trial data, and donated product for trials as needed.
- 3.3.2. **Product modification and suitability:** If barriers (e.g., heat stability in contexts with poor cold chain infrastructure) are identified, but the licensee is unwilling or unable to conduct further R&D and/or bring an alternative to market, the licensee must issue non-exclusive licenses to any interested manufacturer or researcher.

4. Licensing

- 4.1 **Considerations for exclusive vs non-exclusive licensing:** Non-exclusive licensing should be the default. Any departures should be justified and accompanied with a higher threshold of alternative access plans and partnerships. Decisions to permit exclusive licenses should be reviewed by an independently

appointed Access Advisory Council to the NIH (further detailed in the next section).

Accountability, governance, and transparency considerations

5. Oversight

5.1 Establish an NIH Access Advisory Council: An independent oversight body should be established, with careful consideration and avoidance of potential conflicts of interest. The Access Advisory Council should also include a diverse set of experts including those with knowledge of biomedical research, public health, health economics, intellectual property, and licensing practices. Moreover, it should also include at least 2 representatives from underserved populations and LMICs who can provide insight into specific affordability and access challenges. This body should review and approve access plans and waivers ahead of their finalization or NIH final decisions. The Access Advisory Council should review submitted access plans as well as progress reports on the implementation of these plans and provide feedback to improve and strengthen plans.

5.2 Waiver processes:

5.2.1. Providing guidance on the factors considered and process for issuing a waiver: The guidance currently includes provision of partial or whole waivers for access planning, but the guidance at present does not provide needed clarity on a) factors for consideration in issuing the waiver and b) public interest and transparency considerations to allow for wider public feedback.

5.2.2. Transparency: A justification for the issuance of a waiver should be posted to the Federal Register for public notice and comment by third parties. Submitted public comments should be taken into consideration by the NIH Access Advisory Council and NIH in final decision-making.

5.3 Transparency in reporting

5.3.1. Clarify what information should be considered confidential: We commend the guidance for providing that non-confidential versions should be provided by licensees to be provided to the public or third parties. The guidance should be updated to specify that royalty rates, licenses, sublicenses, prices, and progress reports should not be considered as confidential information. Other information that licensees may contend is confidential should be reviewed by the Access Advisory Council before determining whether it is in fact, confidential.

5.4 Amend arbitrary one year rule: The guidance currently includes provisions that licensees meet with NIH to review progress “no more often than once annually.” This is an arbitrary standard, which should be removed. There is no reason for licensees to reasonably expect NIH would seek to meet excessively to merit such

a protection. At a minimum, NIH should meet with licensees annually to review submitted progress reports.

- 5.5 **Provide mechanisms for public feedback:** Progress reports should be made publicly available, and there should be mechanisms in place for the public to provide comments should concerns arise. Public comments should be reviewed by the NIH and the proposed NIH Access Advisory Council, and the NIH should provide public responses to concerns raised, incorporating the Access Advisory Council's position on these concerns as well.

6. Governance and royalties

- 6.1 **Royalties should return to NIH centrally and be re-invested in access activities:** To ensure that individual programs are not disincentivized from pursuing ambitious access plans, royalties should be returned to NIH centrally.

- 6.1.1. **Royalties may be used to finance access plan development,** including independent analysis for COGS, market analysis, and freedom-to-operate in low- and middle-income country jurisdictions.
- 6.1.2. **Royalties may be used to finance access plan monitoring,** including independent evaluations of access plans and their implementation, annual reporting on NIH access achievements and lessons learned, case studies of effective access plans, and an annual award to the NIH Institute with the most successful access plan implementation.
- 6.1.3. **Royalties may be used to finance broader strategic work to improve the NIH access program,** including developing access partnerships and strategically leveraging NIH resources.

7. Long-term strategies for evaluating and improving the effectiveness of access plans

- 7.1 NIH should publicly report on the impact of access plans annually. In 2022, NIH released the commissioned "Public Health and Economic Impact Study of NIH Intramural Technology Transfer Licensing" that included metrics around the effects of NIH-licensed inventions on innovation, economic, and health. The report included several specific metrics related to innovation and economic impacts including commercialization, venture capital investment, regulatory approval, clinical trial activity, sales revenue, tax revenue attribute to sales, labor compensation, and more. The report notably did not include such metrics for health across NIH-licensed inventions, but included case studies and their health impacts for four specific health technologies. Moreover, there were no metrics related to access and affordability as part of the report.

- 7.1.1 **Specific metrics around affordability and access to end products of NIH-licensed inventions in the U.S. and low- and middle-income countries** should be developed and reported on annually as part of the report. The Access Advisory Council could play a role in the development and feasibility testing of such metrics. Data necessary to

measure such metrics could also be asked of licensees in their progress reports as appropriate.

7.1.2 **Case studies of effective access plans to health technologies derived from NIH-funded inventions** should also be included as part of the report. This would provide more insight to taxpayers around NIH's efforts to enable fair returns on their investment and give licensees examples of actionable access plans with public health impact.

7.2 **NIH should also publicly post and update a dashboard around inclusion and implementation of access plans within licenses.** This should include metrics around the number of NIH-licensed inventions with access plans, types of health technologies where such plans have been developed, therapeutic areas for use of the NIH-funded inventions, information around the types of access provisions included within the plans, and status of implementation of access plans. The NIH Access Advisory Council can also provide additional recommendations for what other metrics should be made publicly available through such a dashboard.

8. **Additional considerations for access planning**

8.1 **Besides access to end-products resulting from NIH-licensed inventions, access plans could also include provisions that enable access to research outputs and benefit sharing.** This would include provisions that mandate data sharing from research utilizing NIH-licensed inventions, public access to publications from such research, and collaboration with researchers working within underserved populations in the U.S. and in low- and middle-income countries.

8.2 **NIH could also ensure that third-parties, as well as NIH and other federal agencies, can conduct research of public health importance after commercialization of an end-product derived from an NIH-licensed invention.** This would include postmarketing studies addressing key public health questions that would otherwise remain unanswered, such as comparative effectiveness or efficacy and safety of health technologies within diverse populations. NIH in coordination with other federal agencies including the U.S. Food and Drug Administration and Centers for Medicare and Medicaid Services could also run pragmatic trials to evaluate how such health technologies would be used in the real-world setting, thus providing further evidence around the public health impacts of NIH-licensed inventions (11,12). Moreover, royalties earned from the NIH-licensed inventions should also be utilized to such studies.

8.3 **Enabling continued development of NIH-funded R&D.** Products withdrawn or shelved before market entry should make their testing data publicly available. This would allow not only more efficient use of publicly funded inventions, but also not result in redundant testing of patients, which would be ethically questionable. Such data might be added to various publicly available databases, from NIH's PubChem and the European Union's chEMBL to various NIH Institute clinical trial databases.

We again applaud the NIH for advancing efforts to require licensees of health technologies from the intramural research program to establish access plans. However, the details of this policy are critical in determining whether or not access plans achieve public health impact and fair returns on public investments. For this policy to be meaningful, NIH must set a clear minimum standard for what provisions must be included and implemented by licensees. Moreover, we urge NIH to require that access plans attend to both underserved populations in the U.S. and those in low- and middle-income countries. We recommend that NIH establish an independent Access Advisory Council to ensure adequate oversight around the development and implementation of such plans, while also providing licensees with assistance in doing so. Finally, through transparency of such plans and their impact on access, NIH can also demonstrate the public health and economic benefits to the public of their investment to biomedical research.

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