CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

July 22, 2024

To: National Institutes of Health (NIH) Office of Science Policy (OSP)

From: CIRM Access and Affordability Working Group

Re: Request for Information on Draft NIH Intramural Research Program Policy: Promoting Equity Through Access Planning

The mission of the California Institute for Regenerative Medicine (CIRM) is to accelerate world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world. Since CIRM's inception in 2004, the agency has invested $4.2 billion in regenerative medicine infrastructure, research and education.

CIRM shares NIH's desire to promote access to products resulting from agency-funded biomedical innovation. CIRM's commitment is evidenced by a robust pre-clinical and clinical research portfolio aimed at treating conditions once considered intractable. CIRM's cell and gene therapy manufacturing and clinical networks provide state-of-the-art infrastructure to deliver these new treatments to patients. Working with clinical development teams and our delivery networks CIRM is exploring opportunities to enhance equitable access to treatments.

CIRM thanks NIH for the opportunity to comment on the Office of Science Policy's request for information on the Draft NIH Intramural Research Program Policy: *Promoting Equity Through Access Planning*. The CIRM-team worked with members of a dedicated advisory committee to our governing board: the Access and Affordability Working Group,[1] to draft our response. These comments are the product of the collective insights gained from the development of regenerative medicine research program on the part of CIRM and its partners.

[1] https://www.cirm.ca.gov/board-and-meetings/accessibility-affordability-working-group/

Value in Partnerships

Partnership with patients and patient advocacy organizations is foundational to CIRM. Twelve of the Institute's board members are patient advocates.[1] CIRM has directly and indirectly (through awardee initiatives) formed robust partnerships with non-profits and patient advocacy organizations. In addition, there are two nurse members on CIRM's board providing insights to the unique needs of clinical research. These partnerships have been essential for supporting clinical research as they provide visibility to the populations most likely to benefit from treatments, enable patients to inform protocol design, and facilitate engagement of underserved populations.

Partnering with public health, non-profit, or patient advocacy organizations is an important strategy for addressing patient centered design considerations and providing visibility to clinical research and approved products. CIRM believes there is particular merit in developing robust partnerships to support diversity and inclusion in clinical research.

CIRM recommends Partnering with public health, non-profit, or patient advocacy organizations. Such partnerships may be instrumental in efforts to address structural barriers to access (discussed below).

Accessibility as a Design Objective

CIRM agrees there is an imperative to consider product affordability, availability, acceptability, and sustainability.[2] These considerations are particularly pronounced in the development of regenerative medicine treatments (stem cell and gene therapies). Access planning at the earliest stages of development can serve to address considerations that may influence the market viability of a therapeutic product.

Addressing accessibility as a design objective is an important strategy for acceptable and sustainable development. There are numerous early-stage (pre-clinical) design considerations

[1] https://www.cirm.ca.gov/wp-content/uploads/archive/files/about_cirm/Prop-14-full-text.pdf

[2] The new policy defines "access" broadly to include product affordability, availability, acceptability, and sustainability, is of paramount importance in providing a return on taxpayers' investment in biomedical research.

that may influence the ability to deliver a cell or gene therapy acceptably and sustainably. The FDA has developed numerous guidance document that highlight the importance of design considerations in supporting a Investigational New Drug Application (IND) or a Biologics License Application (BLA).[3] For this reason, CIRM already requests development programs address considerations related to a product's viability, including, materials (e.g. cell line) selection, product processing (Chemistry Manufacturing and Controls) and methods for clinical delivery (efficient and safe approach to product administration (including data-based dosing, dose schedule, and treatment plan) and appropriate long-term monitoring.

CIRM recommends plans for addressing accessibility as a design objective be developed in light of requirements for Investigational New Drug Application (IND) or a Biologics License Application (BLA) and with further consideration to international requirements.

Structural Barriers to Accessing Cell and Gene Therapy Products

The draft policy includes numerous supply-side strategies to support product affordability, availability, acceptability, and sustainability. Many of these strategies make it incumbent on the investigators or sponsors to offer flexible IP or licensing agreement terms. Investigators should consider these strategies in the context of access planning. However, in the context of cell and gene therapies, one must be cognizant of substantial demand-side barriers that potentially limit availability and sustainability of the products of biomedical innovation.

For transformative regenerative medicine treatments there are structural impediments within our health care financing system that potentially inhibit the availability and, potentially, the sustainability of such products. This problem emanates from the fact the market for cell and gene therapies is immature and fragmented. As a consequence, the product's value to the health care system may not be evident to public and private insurers. For example, commenters have noted that current reimbursement policies could reduce patient access to new and innovative medical technologies like CAR T-cell therapies even though the treatments offer superior value over standard of care.[4] Historically, reimbursement has been inadequate to cover

[3] https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/cellular-gene-therapy-guidances
[4] https://www.personalizedmedicinecoalition.org/wp-content/uploads/2023/06/comment-letter.pdf

provider costs.[5] These concerns are compounded for gene therapy products which may require up to 60 days of follow up.[6] Market immaturity also results in uncertainty over the durability of the effect of treatments contributing further uncertainty to a products overall value.[7]
Gene therapy launches must also contend with a variety of complex market institutions, such as the 340b drug pricing program that provides favorable pricing terms to eligible hospitals and clinics, resulting in savings of 25-50%. Cell and gene therapies may limit these discounts.[8] For example, as CMS has explicitly noted, 340b discounts will not apply to sickle cell gene therapy, because it is provided to inpatients and thus not covered by the 340b program.[9] In contrast, many existing sickle cell therapies receive 340b discounts, which could be reduced by transitions to gene therapy.[10] The result is a financial disincentive faced by downstream providers that lies largely beyond the control of the innovator.

Entities with approved products are dedicating substantial resources to documenting the value of new treatments to support reimbursement.[11] CMS recently cited the $2.98 billion per year of sickle cell disease as a rationale for a pilot financing program.[12] Investigators supported by the Intermural Research Program (IRP) often lack the resources to address the range of considerations incumbent in comprehensive health economics and outcomes research. These demand-side considerations may overwhelm the impact of instrumental changes to IP or licensing agreements.

In the context of NIH's efforts to support equitable access to biomedical innovations, we encourage the agency to consider access and affordability infrastructure and initiatives that enable investigators supported by the IRP to effectively demonstrate the value proposition of their products. Specific activities may include the following:

- Value Assessment Infrastructure: Develop support systems or infrastructure to enable researchers to perform health economics and outcomes research (HEOR) during

[5] https://www.hematology.org/advocacy/policy-news-statements-testimony-and-correspondence/policy-news/2019/car-t-cell-therapy-an-update-on-coverage-and-reimbursement
[6] https://www.nejm.org/doi/full/10.1056/NEJMoa2309676
[7] https://icer.org/news-insights/press-releases/icer-and-newdigs-release-white-paper-analyzing-the-challenges-and-potential-policy-options-for-paying-for-gene-therapies/
[8] https://healthpolicy.usc.edu/research/the-340b-drug-pricing-program-background-ongoing-challenges-and-recent-developments/
[9] https://www.cms.gov/cgt-access-model-frequently-asked-questions
[10] https://pubmed.ncbi.nlm.nih.gov/36400534/
[11] https://ashpublications.org/ashclinicalnews/news/7845/Cost-Benefit-Analysis-Favorable-but-Challenging
[12] https://www.cms.gov/files/document/cgt-model-rfa.pdf

clinical development. Information about value is a public good that merits public investments in value assessment.[13] Emphasis should be placed on patient-centered approaches that account for the greater value that patients with severe illness place on improving their health.[14] NIH could encourage and fund these activities in IRP awards, requiring that innovators rely on up-to-date methods that comport with federal prohibitions of discriminating against the aged, sick, and disabled.[15] For instance, a nascent literature has already begun to apply Generalized Risk-Adjusted Cost-Effectiveness (GRACE) to gene therapy.[16]

- Payer Outreach: Support outreach to payers to demonstrate the value of transformative treatments. NIH is uniquely positioned to engage public and private payers around the value of regenerative medicine treatments. Critical to this engagement will be developing consensus on benchmarks for product efficacy and durability; as these factors are central to the value proposition. [17]

- Model Appeals Letters: Utilization Management (UM) models will need to be able to focus specifically upon the patient and the clinical condition that is being treated with a proposed transformative regenerative medicine treatment. In addition, it would be important to ensure that any UM models used in coverage determinations regarding transformative regenerative medicine treatments have sufficient patient protections built into them. This should include the ability of patients to access an expedited appeals process with an independent medical reviewer (with specific expertise in the type of therapeutic and domain of care requested) option should they receive a denial.

[13] https://healthpolicy.usc.edu/research/health-technology-assessment-in-the-u-s-a-vision-for-the-future/
[14] https://www.sciencedirect.com/science/article/abs/pii/S0167629619309208
[15] https://link.springer.com/article/10.1007/s10198-023-01659-7
[16] https://www.ispor.org/docs/default-source/intl2024/grace-scdispor-2024poster138047-pdf.pdf?sfvrsn=efc86964_0
[17] https://icer.org/news-insights/press-releases/icer-and-newdigs-release-white-paper-analyzing-the-challenges-and-potential-policy-options-for-paying-for-gene-therapies/