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October 19, 2026

Office of Science Policy
National Institutes of Health
6705 Rockledge Dr #750
Bethesda, MD 20817

Re: Request for Comment: Draft NIH Biosafety Policy for Research Involving Biohazards (NOT-OD-26-112)

Dear Sir/Madam,

The American Society of Gene & Cell Therapy (ASGCT) appreciates the opportunity to provide comments on the National Institutes of Health's (NIH) *Draft Biosafety Policy for Research Involving Biohazards* (NOT-OD-26-112).

ASGCT is a nonprofit professional membership organization comprised of more than 7,300 scientists, physicians, patient advocates, and other professionals working on cell and gene therapies (CGTs) in settings such as universities, hospitals, and biotechnology companies. The mission of ASGCT is to advance knowledge, awareness, and education that leads to the discovery and clinical application of genetic and cellular therapies to alleviate human disease.

ASGCT acknowledges NIH's stated objectives to modernize biosafety oversight, strengthen research safety, and establish requirements that reflect the evolving biomedical research landscape. We recognize the value of a risk-based oversight framework that maintains appropriate safeguards while reducing unnecessary administrative burden for lower-risk research. However, as NIH considers replacing its longstanding *Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* ("Guidelines"),[1] ASGCT encourages the agency to provide greater clarity regarding the scope and application of the proposed policy, particularly for established research practices and emerging CGT technologies covered by the Guidelines.

Our comments focus on the need for clear, scientifically grounded definitions, consistent compliance expectations, and sufficient implementation guidance to ensure that the new framework supports safe research without introducing unnecessary uncertainty or disruptions to ongoing scientific work.

We offer the following comments regarding the new proposed policy, should replacement Guidelines be finalized:

[1] National Institutes of Health, Office of Science Policy (2024 April). *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*. https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf

1. **Scope of research covered by the new policy, including the definition of biohazards for the purpose of oversight and any inadvertent gaps in oversight that should be addressed.**

ASGCT encourages NIH to clarify the proposed definition of "genetic modification" to ensure it accurately reflects the range of technologies and research activities covered by the policy. As currently written, the definition includes the introduction of nucleic acids that "can be transcribed or translated,"[2] without clearly distinguishing between technologies that permanently alter the genome and those that do not.

This broad language could create confusion regarding the classification of certain technologies, including mRNA-based products, non-integrating gene therapies, and other approaches that introduce genetic material without permanently modifying a recipient's genome. While these technologies that do not modify the genome may warrant appropriate biosafety oversight, the terminology used to describe them should accurately reflect their biological characteristics and intended applications.

ASGCT urges NIH to refine this definition or provide accompanying clarification that distinguishes between the introduction or expression of genetic material, and permanent changes to the genome. Such clarification would help ensure consistent interpretation of the policy while avoiding confusion among researchers, policymakers, and the public. Clear, scientifically grounded terminology is particularly important to maintain public understanding and confidence in emerging biomedical technologies.

2. **Structure of tiered oversight (i.e., Federal, institutional, and investigator), including appropriateness in terms of calibration to risk, accountability measures, transparency, and streamlining of administrative burden, etc.**

Allowing certain activities to undergo delegated Institutional Biosafety Committee (IBC) review could reduce unnecessary administrative burden while maintaining appropriate safety protections. As NIH considers this approach, ASGCT encourages the Institutes to ensure that oversight requirements reflect the actual risks of individual technologies and research activities. CGT research encompasses a broad range of approaches, including viral vectors, genetically modified cells, and other emerging platforms with distinct characteristics and safety profiles.[3,4] Oversight requirements should account for established scientific evidence, prior safety data, and modifications specifically designed to reduce risk, ensuring that the level of review is proportional to the risks of the research – rather than determined solely by broad technology classifications.

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[2] National Institutes of Health, Office of Science Policy (2026 August). *Draft NIH Biosafety Policy for Research Involving Biohazards [NOT-OD-26-112].* https://grants.nih.gov/grants/guide/notice-files/NOT-OD-26-112.html
[3] Ay, C., Reinisch, A. (2025 May). Gene therapy: principles, challenges and use in clinical practice. *Wien. Klin. Wochenschr. 137*(9-10):261-271 https://pubmed.ncbi.nlm.nih.gov/38713227/
[4] Lemmens, M., Dorsheimer, L., Zeller, A., Dietz-Baum, Y. (2024 May). Non-clinical safety assessment of novel drug modalities: Genome safety perspectives on viral-, nuclease- and nucleotide-based gene therapies. *Mutat. Res. Genet. Toxicol. Environ. Mutagen. 896.* https://pubmed.ncbi.nlm.nih.gov/38821669/

ASGCT also encourages NIH to clarify how the proposed oversight framework would interact with existing institutional and FDA requirements for CGT clinical research.[5] Clear expectations and coordination across oversight bodies will be important to avoid unnecessary duplication or delays while maintaining rigorous safety standards.

4. **Effectiveness of compliance and enforcement mechanisms for ensuring biosafety, including strategies for encouraging voluntary compliance for research not subject to the policy (e.g., at non-NIH funded institutions), and addressing any biosecurity challenges.**

ASGCT recognizes the importance of institutional accountability and appropriate enforcement mechanisms to maintain strong biosafety standards. However, the proposed policy's broad scope, coupled with provisions allowing noncompliance to affect current and future NIH funding, raises concerns about the potential consequences of unclear or inconsistently interpreted requirements.

The proposal states that institutions receiving NIH funding must ensure compliance for research conducted or sponsored by the institution, regardless of the individual research project's funding source. It further provides that noncompliance may result in additional funding conditions, termination of awards, or impacts on future funding decisions. Biomedical research programs often require years of continuous effort before meaningful outcomes can be achieved. Long-term preclinical studies, specialized manufacturing facilities, multi-year clinical trials, longitudinal patient follow-up, and complex public-private partnerships cannot be paused and restarted without serious impact on patient participants and institutions. For CGTs, where a single program may span a decade from IND filing to BLA approval,[6,7] mid-stream terminations do not merely delay results. They can end programs entirely. Although similar institutional compliance obligations and funding-related enforcement mechanisms exist under the current Guidelines, the expanded scope of the proposed policy, coupled with the longer development timelines associated with CGTs, makes it especially important that institutions have a clear understanding of their responsibilities.

Without sufficient detail regarding how the new requirements will be interpreted and enforced, researchers and institutions may face uncertainty about whether established practices remain compliant. This uncertainty could discourage research activities, create unnecessary administrative burden, or disrupt ongoing projects, even where there is no meaningful change in biosafety risk. Nearly every FDA-approved CGT available to patients today traces its origins to decades of federally supported scientific research.[8] Maintaining consistency and predictability in

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[5] Food and Drug Administration (2026). *Cellular & Gene Therapy Guidances*. https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/cellular-gene-therapy-guidances

[6] Elsallab, M., Ouvina, M., Arfe, A., Bourgeois, F. (2024) Mapping the Clinical Development Trajectory of Cell and Gene Therapy Products. *Clin Pharmacol Ther 117*(5). https://pmc.ncbi.nlm.nih.gov/articles/PMC12447590/

[7] Lapteva, L., Purohit-Sheth, T., Serabian, M., Puri, R. (2020 October). Clinical Development of Gene Therapies: The First Three Decades and Counting. *Mol Ther Methods Clin Dev*. https://pmc.ncbi.nlm.nih.gov/articles/PMC7658574/

[8] Cleary, E., Jackson, M., Zhou, E., Ledley, F. (2023 April) Comparison of Research Spending on New Drug Approvals by the National Institutes of Health vs the Pharmaceutical Industry, 2010-2019. *JAMA 28*(4). https://pmc.ncbi.nlm.nih.gov/articles/PMC10148199/

federal research funding is essential to sustain the basic research that has helped produce today's pipeline of more than 4,400 therapies.[9]

ASGCT therefore encourages NIH to establish clear, consistent, and transparent compliance standards *before* implementing any new policy. Enforcement should be proportional to the nature and severity of a violation, with appropriate opportunities for institutions to identify and correct deficiencies. An explicit appeals process would help mitigate some of the uncertainty around the policy's implementation. Given that the detailed examples and guidance in the current Guidelines would be removed, NIH should ensure that any appeals process is clearly defined and fully transparent. NIH should also clarify how compliance concerns involving individual research activities would be evaluated and ensure enforcement actions do not unnecessarily jeopardize unrelated programs or funding under an institution's broader research portfolio.

These safeguards would help ensure that biosafety oversight remains focused on protecting researchers and the public while providing institutions with the predictability needed to plan and conduct biomedical research.

5. Feedback on the implementation resources and areas in which additional guidance would be beneficial.

ASGCT is concerned that the proposed policy substantially reduces the level of detail contained in the Guidelines. Currently, there are extensive examples, definitions, and specific requirements that researchers and institutions have relied upon to determine appropriate biosafety practices. While a more streamlined policy may offer some benefit, removing this detail without providing comparable guidance could create uncertainty regarding how established research activities will be evaluated under the new framework.

For CGT researchers, this uncertainty may be particularly consequential given the diversity of technologies and research approaches used across the field. ASGCT encourages NIH to retain or replace the practical examples and technical guidance provided under the existing Guidelines, including clear explanations of how the new requirements apply to research already being conducted. Broad or opaque application of the new guidelines may discourage institutions from undertaking ambitious, high-investment projects. It could make it harder to attract partnerships that translate federal discoveries into domestic manufacturing. The more limited detail in this new policy could be particularly damaging to emerging investigators and early-career scientists, who may require more guidance on emerging technologies and best practices. In particular, NIH should issue implementation resources that clarify whether and how established research practices will be affected by the transition to the new policy.

Finally, ASGCT reemphasizes the importance of providing sufficient implementation guidance *before* the new policy takes effect. We encourage NIH to make these materials available for public review before finalizing or implementing the policy, particularly where they will determine how existing research practices are classified and overseen. Detailed examples, frequently asked questions, and guidance addressing common CGT research activities would help

[9] American Society of Gene and Cell Therapy, Citeline (2026). Gene, Cell, & RNA Therapy Landscape Report: Q2 2026 Quarterly Data Report. https://www.asgct.org/uploads/files/general/Final-ASGCT-Citeline-Q2-2026.pdf

institutions prepare for the transition. NIH should also consider whether the proposed six-month implementation period provides sufficient time for institutions to evaluate existing research, update procedures, and ensure compliance without interrupting ongoing studies.

Conclusion

ASGCT recognizes NIH's efforts to modernize biosafety oversight and the importance of maintaining appropriate protections for researchers, patients, and the public. Any updated framework should provide clear, scientifically grounded expectations that reflect advances in biomedical research - while allowing established and emerging technologies to be evaluated according to their actual risks.

As NIH reviews feedback on the proposed new policy, ASGCT urges the agency to clarify the definition of genetic modification, preserve practical guidance for established research activities, and establish transparent, proportional compliance and enforcement expectations. We further encourage NIH to engage with researchers, institutional biosafety professionals, and other stakeholders to ensure that the final policy and accompanying implementation resources are clear, workable, and supportive of continued scientific innovation.

ASGCT appreciates the opportunity to provide these comments and looks forward to continued engagement with NIH on policies that support safe, responsible, and innovative biomedical research. If you would like to hear more from ASGCT's member experts, please reach out to Caitlin McCombs, ASGCT's public policy manager at cmccombs@asgct.org.

Sincerely,

David Barrett, JD, MS
Chief Executive Officer
American Society of Gene and Cell Therapy