Science Advancement & Outreach
A DIVISION OF PETA

1536 16th St. N.W., Washington, DC 20036

October 12, 2026

Dear members of the National Heart, Lung, and Blood Advisory Council,

I'm writing on behalf of Science Advancement and Outreach, the biomedical science policy division of People for the Ethical Treatment of Animals. We appreciate that the National Heart, Lung, and Blood Institute (NHLBI) has released new guidance on applications proposing the use of animals, including requiring more transparency and a plan to validate findings from animal experiments in human models.[1] We also appreciate that NHLBI is funding innovative, non-animal research projects.

These are positive steps, but they are the bare minimum. NHLBI must stop funding experiments on animals that have a poor record of translational value and do not align with the goals of the agency, the administration, or the public.

In this vein, we continue to request that the Council advise NHLBI to stop conducting and funding sepsis research that uses other animals and redirect resources to support sepsis research and training focused exclusively on non-animal methods.

As we presented in our oral comment to you in your last meeting on June 9, 2026, more than 150 drugs for human sepsis that appeared promising in preclinical animal testing have failed in clinical trials.[2,3] These repeated failures reflect major biological differences between humans and the species used in sepsis experiments,[4,5,6,7,8,9,10,11] as well as the inability of preclinical sepsis-inducing methods[12,13] and laboratory conditions[14,15,16,17] to accurately reproduce human disease onset and progression.

NHLBI must follow the National Institute of General Medical Sciences' lead in relegating rodent models of sepsis as "low priority",[18] discouraging their use, and encouraging investigators to use non-animal methods.[19]

To develop safe, effective interventions for patients with sepsis, research must be grounded in human biology—not in approximations derived from fundamentally different species. Importantly, recent analyses have pointed out that "making animal studies more careful and rigorous tends to show that their results predict human outcomes even less well than was thought"[20] and "such efforts have not translated into lower overall clinical failure rates."[21]

NHLBI is currently funding at least 49 projects using mice in attempts to model human sepsis and sepsis-induced complications (see Appendix A for a list). NHLBI has awarded

more than $122 million to these projects, which have little to no chance of advancing treatments for sepsis and related complications. <u>The Council must push for a change.</u>

Non-animal methods, including organoids,[22] microfluidic systems,[23,24] genomics,[25,26] and machine learning and other artificial intelligence tools,[27,28] are already advancing sepsis research. These tools are grounded in human biology and offer greater translational relevance than animal models, but they remain dramatically underfunded and underutilized.

Recognizing the need to move away from animal use and the promise of human-based approaches, all major government entities in the U.S. have initiated plans to reduce animal testing and increase support of non-animal methods.[29,30] NHLBI can leverage this effort and align with the NIH Unified Strategy[31] to drive progress by expanding training and funding opportunities for NAMs so that researchers can better understand and use them in sepsis research. This could include:

- training grants and fellowships focused on human-based approaches,
- education programs developed in partnership with universities and research institutes,
- transition awards for researchers looking to switch from animal experiments to human-based methods,
- and early-career awards to support scientists who wish to begin a fruitful career in human-based sepsis research.

Most NIH-funded basic, translational, and preclinical researchers continue to receive training primarily in animal-based methods, with limited exposure to human-based approaches. In addition, transitioning to these methods can require significant investment in new infrastructure, retraining, and interdisciplinary collaboration. Targeted support from NHLBI would help address these barriers and support wider adoption across the research community.

These recommendations are detailed further in our policy roadmap, Research Modernization NOW,[32] including a dedicated section on sepsis.[33] By implementing these recommendations, NHLBI will lead NIH in prioritizing human-based research, advancing more predictive and human-relevant science, and accelerating progress toward effective sepsis treatments and improved patient outcomes.

Thank you for your time and consideration. We welcome the opportunity to discuss these recommendations further.

Sincerely yours,



Frances Cheng, PhD
Senior Scientist

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Appendix A: A list of NHLBI-funded projects on sepsis and sepsis-induced complications using mice that are active as of October 2026

1. Anderson EJ. Determinants of cardioprotection by circulating prohibitin-1 during sepsis. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11309589
2. Ansari SA. Lipid peroxidation- and pyroptosis-induced tissue factor activation in pathogen-induced blood coagulation. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11514482
3. Aslaner D. Attenuation of sepsis-induced microvascular permeability and inflammation with the GLP-1R agonist liraglutide. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11389192
4. Bapat A. WNT Signaling in the Pathogenesis of Atrial Fibrillation. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11399723
5. Bhattacharya J. Mechanistic role of membrane pore formation in lung-endothelial barrier failure due to blood-borne pathogens. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11171649
6. Birukova A, Hong CC. GPR68 as a novel modulator of septic lung injury. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11384163
7. Black SM. Mito-inflammation and sepsis-induced acute lung injury. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11397282
8. Bosmann M. PACC1 in host defense against bacterial infections and sepsis. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11368037
9. Cater D. In-vivo and Ex-vivo Analysis of Tissue S-nitrosothiols in Sepsis. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11302338
10. Evans CE. Inhibiting Endothelial Apoptosis in Sepsis-Induced Lung Injury. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11363856
11. Fan GC. CPNE5 in Cardiovascular Barrier Dysfunction and Septic Cardiomyopathy. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11419035

12. Fan GC. Lcn10 in Sepsis-Induced Vascular Leakage and Heart Failure. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/10986114
13. Fazal F, Rahman A. MAM Proteins in Lung Vascular Injury. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11370574
14. Garo LP. The Role of Proton-Activated Chloride Channel 1 (PACC1) in Bacterial Pneumonia and Sepsis. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11395530
15. Gollomp K. NET stabilization: mechanistic and therapeutic studies studying the role of NETs in thromboinflammatory disease. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11304516
16. Gumbiner BM. Novel Mechanisms Controlling Endothelial Junctions and Vascular Permeability. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11096007
17. Herson PS, Schmidt EP. Vascular mechanisms of sepsis-induced cognitive dysfunction. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11289469
18. Hu G. ER-phagy regulation of immune response: mechanisms and significance. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11380930
19. Huang W. Mitochondrial R-loop in sepsis-induced cardiomyopathy. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11299483
20. Isakson BE, Koval MH. Purinergic Regulation of Veinous Endothelial Permeability. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11364179
21. Kalinichenko V, Kalin T. Improving endothelial repair in pediatric ARDS. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11444432
22. Khasawneh FT. Characterization of RGS Function and Signaling. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11387365
23. Kim M, Pietropaoli AP. Complement C1q and sepsis associated fatalities. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11122274
24. Knepper M. Solute And Water Transport In Renal Epithelia. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11398507
25. Kron IL, Laubach VE, Yang Z. Targeted treatment of acute lung injury using isolated lung perfusion. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11230212
26. Lamb FS, Stark RJ. The Contribution of Superoxide Influx via LRRC8 Anion Channels to Infectious Vascular Dysfunction. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11297451
27. Li Y, Meng Q. A Lung-Specific, Sulfonium Lipid Nanoparticle (sLNP) Formulation of Incyclinide for the Treatment of ALI/ARDS. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11406986
28. Mangalmurti NS. Determining the role of RBCs in sepsis heterogeneity. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11274869
29. Mangalmurti NS. Investigating the function of RBC-TLR7 in Sepsis. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11323567
30. McGuffee R. The Role of Plasmalogen Mitochondrial and Endothelial Antioxidant Properties in Sepsis. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11176213

31. McMahon TJ, Doctor A. Red blood cell ATP export and transfusion in sepsis. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11289340
32. Mensah S. The Role of the Endothelial Glycocalyx in Sepsis-Induced Coagulation. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11444736
33. Middleton EA. Lung megakaryocytes and lung megakaryocyte-derived platelets contribute to lung injury. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11284994
34. Minshall RD, Karginov AV. Gα12-dependent mechanisms of basal and regulated endothelial cell vWF secretion. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11359343
35. Morley SC. Novel coenzyme Q6 variant reveals non-immune determinants of survival during pneumococcal sepsis. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11393768
36. Radbel JM. Mechanisms underlying susceptibility to ozone-induced ARDS. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11274655
37. Rosenblum SL. Iron deficiency worsens endothelial cell pathology and potentiates inflammatory tissue injury. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11313580
38. Shridas P. Investigating the Role of HDL-Associated Serum Amyloid A in Sepsis-Induced Acute Lung Injury and Mortality. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11252301
39. Suber TL. Intrapulmonary itaconate as a host-protective metabolite during ER Stress and Klebsiella pneumoniae infection. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11322636
40. Surve MV. Functions and Mechanisms of Lung Microfold cells during Invasive Pneumococcal Disease. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11171470
41. Trzeciak AJ. WNK1-dependent macropinocytosis mediates emergency myelopoiesis. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11552997
42. Verin AD, Su Y. Calpain/talin/MLCP axis in pulmonary endothelial barrier regulation. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11192837
43. Walker WE. Adverse effects of sepsis on sleep: a bi-directional interaction. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11463237
44. Wang P. Improvement of Organ Function after Severe Hypovolemia. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11249607
45. Wang Y. The vital role of T403 phosphorylation of STAT2 in post-viral bacterial pneumonia. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11304498
46. Wu R. Role of MMP3 in cardiac microvascular barrier dysfunction and heart failure during sepsis. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11576508
47. Zhao TC. Deltex E3 ubiquitin ligase 3L: A novel mechanism and protective approach in sepsis. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11428083

48. Zhao Y. Novel intrinsic endothelial stem cells responsible for lung endothelial regeneration and vascular repair in ARDS. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11251790
49. Zhao Y. Targeting inflammaging to inhibit endothelial injury and ARDS development in aging lungs. https://reporter.nih.gov/search/7tgatSLH2k2ASbZmQmjp8Q/project-details/11431171