Science Advancement & Outreach
A DIVISION OF PETA

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

May 13, 2026

Dear members of the National Diabetes and Digestive and Kidney Diseases Advisory Council:

On behalf of Science Advancement and Outreach, the biomedical science policy division of People for the Ethical Treatment of Animals, I write to request that the Council advise the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to prioritize and support sepsis research and training focused exclusively on non-animal methods, and to end the conduct and funding of sepsis research that uses other animals.

1. **End the use of animals in sepsis research**

Despite having passed preclinical efficacy and safety testing in animals, 100% of new drugs for sepsis (at least 150 drugs)[1,2] have failed in human clinical trials.[3] This high drug failure rate can be mainly attributed to the numerous biological differences between humans and other animals used in sepsis experiments,[4,5,6,7,8,9,10,11] along with the inability of sepsis inducing methods[12,13] and laboratory conditions[14,15,16,17] to replicate human sepsis onset and progression. As such, it is clear that sepsis experiments that use animals are preventing the development of safe and effective treatments for human sepsis, wasting time, funding, and intellectual resources.

In response, a 2019 working group on sepsis convened by the National Institute of General Medical Sciences (NIGMS) recommended that the institute rebalance its sepsis research portfolio to place a greater emphasis on clinical research.[18] NIGMS accepted this recommendation and subsequently issued a notice of information stating it would now consider "rodent models of sepsis" to be "of low priority."[19] At the 2025 Shock Society Annual Meeting, a NIGMS official reiterated that NIGMS is "not a fan" of rodent models of sepsis and encouraged investigators to seek access to human samples, noting that human-based research is "a way for the future that everyone sees coming and thinks is good."[20]

According to NIH RePORTER, NIDDK is currently funding at least 10 projects that use mice in sepsis-related experiments. We urge NIDDK to not renew funding for these and other projects that use mice and other animals in attempts to model human sepsis and redirect resources toward human-relevant, non-animal approaches, as NIGMS has done.

2. **Expand training and opportunities for sepsis researchers using non-animal methods**

Non-animal technologies are already demonstrating their value, generating important discoveries in sepsis research. Advanced human tissues models are being used to study sepsis pathogenesis,[21]

while microfluidic systems are enabling the analysis of patient blood samples for sepsis biomarker identification.[22,23] Additionally, advances in genomics[24,25] and AI/machine learning[26,27] are improving sepsis diagnosis and prognosis.

To sustain and accelerate this progress, NIDDK must invest in initiatives like those suggested below to give non-animal researchers the support they need:

- Provide training grants and fellowships that equip researchers with the skills needed to apply non-animal methodologies in sepsis research
- Partner with universities and research institutes to establish continuing education and certification programs focused on non-animal approaches for sepsis research
- Offer transition and early-career awards to support investigators in replacing sepsis animal experiments with human-based systems and establishing human-focused research programs.

Most NIH-funded researchers continue to receive training primarily in animal-based methods, with limited exposure to non-animal approaches. In addition, transitioning to these methods can be challenging due to the costs associated with retraining, acquiring new laboratory infrastructure, and accessing interdisciplinary expertise (e.g., bioengineering and computational modeling). By providing the above opportunities, NIDDK can ensure that its intramural and extramural researchers are equipped with the skills and resources needed to implement and advance human-relevant sepsis research.

These and related recommendations are expanded on in our policy roadmap, Research Modernization NOW, now available in a web format, including a dedicated section on sepsis.

By implementing these recommendations, NIDDK will not only align with NIH's Unified Strategy[28] but also advance more predictive and human-specific research that will accelerate progress toward effective sepsis treatments and improved patient outcomes.

Thank you for considering these recommendations.

Sincerely,

Gabby Vidaurre, Ph.D.
Research Associate

[1] Seok, et al. Seok J, Warren HS, Cuenca AG, et al. Genomic responses in mouse models poorly mimic human inflammatory diseases. *Proc Natl Acad Sci U S A*. 2013;110(9):3507-3512. doi:10.1073/pnas.1222878110

[2] Collins F. Of mice, men, and medicine. NIH. February 19, 2013. Accessed May 5, 2026. https://us.pagefreezer.com/en-US/wa/browse/c530da90-f454-461b-9a86-959c53acb16c?url=https:%2F%2Fdirectorsblog.nih.gov%2F2013%2F02%2F19%2Fof-mice-men-and-medicine%2F&timestamp=2025-05-27T10:13:51Z

[3] NAGMSC. NAGMSC Working Group on Sepsis final report. May 17, 2019. Accessed May 5, 2026. https://www.nigms.nih.gov/sites/nigms/files/migrated/nagmsc-working-group-sepsis-report.pdf

[4] Seok, et al.

[5] Fink MP. Animal models of sepsis. *Virulence*. 2014;5(1):143-153. doi:10.4161/viru.26083

[6] Hawash MBF, Sanz-Remón J, Grenier JC, et al. Primate innate immune responses to bacterial and viral pathogens reveals an evolutionary trade-off between strength and specificity. *Proc Natl Acad Sci U S A*. 2021;118(13):e2015855118. doi:10.1073/pnas.2015855118

[7] Bjornson-Hooper ZB, Fragiadakis GK, Spitzer MH, et al. A comprehensive atlas of immunological differences between humans, mice, and non-human primates. *Front Immunol*. 2022;13:867015. doi:10.3389/fimmu.2022.867015

[8] Mair KH, Sedlak C, Käser T, et al. The porcine innate immune system: an update. *Dev Comp Immunol*. 2014;45(2):321-343. doi:10.1016/j.dci.2014.03.022

[9] Meurens F, Summerfield A, Nauwynck H, Saif L, Gerdts V. The pig: a model for human infectious diseases. *Trends Microbiol*. 2012;20(1):50-57. doi:10.1016/j.tim.2011.11.002

[10] Chalupova M, Horak J, Kramna L, et al. Gut microbiome diversity of porcine peritonitis model of sepsis. *Sci Rep*. 2022;12(1):17430. doi:10.1038/s41598-022-21079-6

[11] Redl H, Bahrami S. Large animal models: baboons for trauma, shock, and sepsis studies. *Shock*. 2005;24 Suppl 1:88-93. doi:10.1097/01.shk.0000191339.46777.63

[12] Ruiz S, Vardon-Bounes F, Merlet-Dupuy V, et al. Sepsis modeling in mice: ligation length is a major severity factor in cecal ligation and puncture. *Intensive Care Med Exp*. 2016;4(1):22. doi:10.1186/s40635-016-0096-z

[13] Joffre J. Preclinical model in sepsis: should we abandon the CLP? *J Inflamm Res*. 2023;16:1757-1759. doi:10.2147/JIR.S415972

[14] Esmon CT. Why do animal models (sometimes) fail to mimic human sepsis? *Crit Care Med*. 2004; 32(5 Suppl):S219-222. doi:10.1097/01.ccm.0000127036.27343.48

[15] Rittirsch D, Hoesel LM, Ward PA. The disconnect between animal models of sepsis and human sepsis. *J Leukoc Biol*. 2007;81(1):137-143. doi:10.1189/jlb.0806542

[16] Buras JA, Holzmann B, Sitkovsky M. Animal models of sepsis: setting the stage. *Nat Rev Drug Discov*. 2005;4(10):854-865. doi:10.1038/nrd1854

[17] Nemzek JA, Hugunin KMS, Opp MR. Modeling sepsis in the laboratory: merging sound science with animal well-being. *Comp Med*. 2008;58(2):120-128

[18] NAGMSC

[19] National Institute of General Medical Sciences. Notice of information: NIGMS priorities for sepsis research. July 29, 2019. Accessed May 5, 2026. https://grants.nih.gov/grants/guide/notice-files/NOT-GM-19-054.html

[20] Trunnell ER. Science Advancement & Outreach at the Shock Society Annual Conference in Boston. Science Advancement & Outreach. June 2025. Accessed May 5, 2026. https://www.scienceadvancement.org/reflections/sao-at-shock-con-2025/

[21] Li Y, Nie Y, Yang X, et al. Integration of Kupffer cells into human iPSC-derived liver organoids for modeling liver dysfunction in sepsis. *Cell Rep*. 2024;43(3):113918. doi:10.1016/j.celrep.2024.113918

[22] Yang X, Pu X, Xu Y, et al. A novel prognosis evaluation indicator of patients with sepsis created by integrating six microfluidic-based neutrophil chemotactic migration parameters. *Talanta*. 2025;281:126801. doi:10.1016/j.talanta.2024.126801

[23] Griffin K, Miller L, Yang Y, et al. Affinity-based 3D-printed microfluidic chip for clinical sepsis detection with CD69, CD64, and CD25. *J Pharm Biomed Anal*. 2025;252:116500. doi:10.1016/j.jpba.2024.116500

[24] Burnham KL, Milind N, Lee W, et al. eQTLs identify regulatory networks and drivers of variation in the individual response to sepsis. *Cell Genom*. 2024;4(7):100587. doi:10.1016/j.xgen.2024.100587

[25] Harris PNA, Bauer MJ, Lüftinger L, et al. Rapid nanopore sequencing and predictive susceptibility testing of positive blood cultures from intensive care patients with sepsis. *Microbiol Spectr*. 2024;12(2):e0306523. doi:10.1128/spectrum.03065-23

[26] Steinbach D, Ahrens PC, Schmidt M, et al. Applying machine learning to blood count data predicts sepsis with ICU admission. *Clin Chem*. 2024;70(3):506-515. doi:10.1093/clinchem/hvae001

[27] Boussina A, Shashikumar SP, Malhotra A, et al. Impact of a deep learning sepsis prediction model on quality of care and survival. *NPJ Digit Med*. 2024;7(1):14. doi:10.1038/s41746-023-00986-6

[28] National Institutes of Health. Advancing NIH's mission through a unified strategy. August 15, 2025. Accessed May 5, 2026. https://www.nih.gov/about-nih/nih-director/statements/advancing-nihs-mission-through-unified-strategy