Science Advancement & Outreach
A DIVISION OF PETA

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Oral comments for the National Heart, Lung, and Blood Advisory Council meeting:

Thank you for the opportunity to comment on behalf of Science Advancement and Outreach, the biomedical science policy division of People for the Ethical Treatment of Animals. We request that the Council advise the National Heart, Lung, and Blood Institute 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.

More than 150 drugs for human sepsis that appeared promising in preclinical animal testing have failed in clinical trials.[1,2] These repeated failures reflect major biological differences between humans and the species used in sepsis experiments,[3,4,5,6,7,8,9,10] as well as the inability of preclinical sepsis-inducing methods[11,12] and laboratory conditions[13,14,15,16] to accurately reproduce human disease onset and progression.

In response to these translational failures, a 2019 National Institute of General Medical Sciences working group recommended rebalancing sepsis research toward a stronger clinical focus.[17] NIGMS later described rodent models of sepsis as "low priority."[18] Just last year, an NIGMS representative reaffirmed that the agency is "not a fan" of the most commonly used animal models of sepsis (such as cecal ligation and puncture and LPS injection), and encouraged investigators to use human-based research, as it represents "the future" of the field. NIGMS encouraged scientists to think critically about their models and avoid "just going back and doing something in a lab in a way that's easy or was done that way in the past."[19]

NHLBI must follow NIGMS' lead.

NIH RePORTER shows that NHLBI is currently funding at least twenty-six projects using mice in attempts to model human sepsis. The Council must push for a change.

Non-animal methods are already advancing sepsis research. Human tissue models are being used to study disease mechanisms;[20] microfluidic systems are enabling biomarker discovery from patient blood samples;[21,22] and advances in genomics,[23,24] artificial intelligence, and machine learning[25,26] are improving both diagnosis and prognosis. These tools are grounded in human biology and offer greater translational relevance than animal models, but they remain dramatically underutilized relative to their potential.

To accelerate progress, NHLBI should expand training and funding opportunities so that researchers can better understand and know how to use non-animal methods in sepsis research. This could include training grants and fellowships focused on human-based approaches, continuing education programs developed in partnership with universities and research institutes, and transition and early-career awards to support investigators who either wish to replace animal experiments with non-animal systems or 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*, available at science.peta.org, including a dedicated section on sepsis.

By implementing these changes, NHLBI will align with the NIH Unified Strategy[27] while advancing more predictive, human-relevant science and accelerating progress toward effective sepsis treatments and improved patient outcomes.

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

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