**UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF MARYLAND**

**PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS, INC.**
501 Front Street
Norfolk, Virginia 23510,

Plaintiff,

v.

**DR. FRANCIS COLLINS**, in his official capacity as Director of the National Institutes of Health,
**9000 Rockville Pike**
**Bethesda, Maryland 20892**

**NATIONAL INSTITUTES OF HEALTH**
9000 Rockville Pike
Bethesda, Maryland 20892,

**XAVIER BECERRA**, in his official capacity as Secretary of the United States Department of Health and Human Services,
200 Independence Avenue SW
Washington DC 20201

and

**UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES**
200 Independence Avenue, S.W.
Washington, D.C. 20201,

Defendants.

**Civ. No. _____**

**COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF**

## INTRODUCTION

1. Pursuant to the Administrative Procedure Act ("APA"), 5 U.S.C. §§ 551 *et seq.*, 701 *et seq.*, Plaintiff People for the Ethical Treatment of Animals, Inc. ("PETA") challenges final agency actions by the National Institutes of Health ("NIH"), an agency of the United States Department of Health and Human Services ("HHS"), namely the NIH's approval of grants for

sepsis experiments on mice and other animals. The NIH is authorized to fund research for the benefit of human health, and it has known since at least 2013 that mice do not experience human sepsis, as NIH Director Dr. Francis Collins acknowledged in February of that year, exclaiming "No wonder drugs designed for the mice failed in humans: they were, in fact, treating different conditions!" Despite both this knowledge and its statutory funding purpose of improving *human* health (*see* 42 U.S.C. § 241(a)), the agency continues to sidestep the parameters of its authority and fund animal-sepsis experiments that have proven futile for human health, spending more than $20 million for new projects in the past twenty months and at least $10 million for new projects in fiscal year 2021. The NIH funds the majority of basic medical research in the United States, such as the kind of sepsis experimentation described herein.

2. In a typical year, sepsis afflicts at least 1.7 million American adults and kills nearly 270,000 Americans, and one of every three patients who dies in a hospital has sepsis. It is the body's extreme response to an infection and can quickly cause tissue damage and organ failure. Considering the gravity of sepsis in the United States, research relevant for its treatment should be a priority of the agency, which describes itself as the nation's "steward" of medical research.

3. *No* new pharmacological treatments have been developed for sepsis, despite decades of intensive study. NIH has spent billions of taxpayer dollars on animal-sepsis experiments that, while failing to help humans, are painful, debilitating, and fatal for the animals used. Indeed, there is no specific, targeted pharmacologic treatment for human sepsis of any form.

4. The agency's entrenchment in a research model that it has acknowledged does not accurately replicate the disease that humans experience, and that, despite decades of research, has failed to result in any treatment for humans with sepsis, goes beyond poor stewardship to deliberate actions to exercise its statutory authority in a manner that is outside the bounds of its mandate.

5. While NIH continues to approve grants for experiments it declared in 2013 to be fundamentally removed from human health, human-relevant approaches to studying sepsis that do not use animals are available and are showing promise. NIH's reliance on unreliable, unproductive animal-sepsis experiments has left human sepsis patients without a targeted treatment for this deadly condition.

6. In 2019, the NIH's primary funder of sepsis research, the National Institute of General Medical Sciences, reiterated the conclusion that research on animals has consistently failed to help humans suffering from sepsis and that the larger scientific community doubts the usefulness of rodents in developing a treatment for human sepsis. Nonetheless, the NIH continues to award grants for such experiments, including those that do not even attempt to correct particular well-documented shortcomings.

7. The NIH's statutory funding authority is restricted to research that affects *human* impairments, and the agency must satisfy particular statutory and regulatory directives in exercising its authority. Sepsis in animals is not human sepsis; they are different conditions, and the findings generated from experiments on mice and other animals do not translate into treatments for human sepsis patients. For NIH to acknowledge this in 2013 yet continue to award grants for animal-sepsis experiments that it knows are inherently ill-suited to develop a treatment for sepsis in humans is arbitrary, capricious, an abuse of discretion, not in accordance with law, and in excess of statutory jurisdiction, authority, or limitations within the meaning of the Administrative Procedure Act ("APA"), 5 U.S.C. § 706(2)(A), (C).

## JURISDICTION, VENUE, AND RELIEF

8. This Court has jurisdiction over the subject matter of the Complaint pursuant to 28 U.S.C. § 1331 because this action constitutes a federal question under the APA, 5 U.S.C. §§ 551-559, 701-706.

9. Venue is proper in this Court under 5 U.S.C. § 552(a)(4)(B) and 28 U.S.C. § 1391(e) because the agency records are situated in this District, a substantial part of the events giving rise to this action occurred in this District, and a Defendant, the NIH, resides in this District.

10. The challenged agency actions are final and, therefore, subject to judicial review pursuant to 5 U.S.C. §§ 702, 704, and 706.

11. Declaratory relief is authorized by 28 U.S.C. §§ 2201 and 2202. Injunctive relief is authorized by Federal Rule of Civil Procedure 65 and the APA, 5 U.S.C. § 706.

## PARTIES

**Plaintiff**

12. Plaintiff is a non-profit organization headquartered in Norfolk, Virginia, that is dedicated to protecting animals from abuse, neglect, and cruelty. PETA undertakes these efforts through, *inter alia*, public education, investigations, research, animal rescue, legislation, special events, celebrity involvement, and protest campaigns.

13. The primary focus of PETA's mission is advocacy on behalf of animals used in experimentation. A critical component of that focus is PETA's work to facilitate the development and adoption of human-relevant methods of studying and treating human disease, including by providing funding, presenting at scientific conferences, authoring scientific papers, submitting shareholder resolutions, and collaborating with corporations and regulatory agencies to accept non-animal tests on a product's safety—work that also contributes to reducing the numbers of

animals used in experimentation. As part of its primary mission, PETA also advocates for reducing pain and distress in animals used in experimentation, including by communicating directly with research facilities about their treatment of animals and filing complaints with state and federal agencies.

14. To fulfill its mission, PETA spends substantial resources each year advocating on behalf of animals used in experimentation, including sepsis experimentation.

15. Scientists on PETA's staff analyze voluminous government records, scholarly articles, and other documents and studies and synthesize such materials for dissemination and for advocacy directed toward government bodies, research facilities, and other members of the scientific community.

16. PETA collaborates on, promotes, and funds the development and use of human-relevant, non-animal research approaches and presents information on such methods to the NIH, research facilities, the scientific community, and the general public.

17. PETA investigates complaints about laboratories' violations of state and federal law submitted by members of the public, including whistleblowers.

18. PETA uses its website, publications, and the media to disseminate information to its members and the general public about government actions affecting animals, including animals used in experimentation.

19. PETA routinely sends correspondence and reports to the government concerning experiments on animals, alternatives to the same, and violations of federal law at facilities receiving federal funding.

20. PETA engages with private companies using or funding experiments on animals in order to foster the use and development of non-animal methods of experimentation and facilitate the disuse of failed animal models.

21. PETA responds to requests for public comment from federal agencies concerning experimentation on animals. PETA's members also routinely comment on such matters.

22. The NIH's actions to award federal funding for animal-sepsis experiments as addressed in this Complaint, in spite of its longstanding knowledge that the experiments being funded do not advance the NIH's statutory directive to fund research for the benefit of human health, and in spite of PETA's repeated correspondence with the agency, frustrate and are directly contrary to PETA's mission. PETA advocates for scientifically sound, human-relevant research methods that do not harm animals. By ignoring its knowledge of the fundamental flaws in animal-sepsis experiments and continuing to fund awards for such experiments, the NIH contravenes its statutory funding authority and its own funding criteria and thereby compels PETA to spend more resources educating the public about, and bringing to the agency's attention, the futility of such taxpayer-funded experiments, particularly given the availability of human-relevant, non-animal approaches to sepsis research.

23. PETA has spent considerable resources monitoring and analyzing the use of animals in animal-sepsis experimentation and writing the NIH about the wasteful use of taxpayer dollars on such experiments. PETA has used and will continue to use its website, publications, and the media to disseminate information about such experiments and human-relevant methods of studying human sepsis. PETA has advocated and will continue to advocate for a decrease in the use of animals in sepsis experimentation and for a greater focus on human-relevant approaches. For example, among other activity, PETA has conducted an eyewitness investigation

of sepsis experiments at the University of Pittsburgh that led one veterinarian to describe mice inflicted with the condition as "falling over dead" in their cages and subsequently engaged in direct outreach to the university and public demonstrations; repeatedly written the NIH regarding the failings of sepsis experimentation on animals and to implore the agency to redirect its funding to human-relevant, non-animal research methods; presented the case against using animals in sepsis experiments at a scientific conference; organized PETA's members and supporters to email the NIH with messages of support for humane and human-relevant sepsis research; demonstrated outside HHS and elsewhere to urge the cessation of funding of fruitless sepsis experiments on animals and a focus instead on funding research that is useful for human health; and submitted Freedom of Information Act requests regarding sepsis experiments on animals and disseminated the responsive public records and videos of experiments. PETA will continue to undertake the above referenced actions.

24. PETA has been and will continue to be harmed by the NIH's actions in continuing to fund animal-sepsis experiments despite the overwhelming evidence that such experiments do not satisfy the agency's authority to use taxpayer resources for the advancement of *human* health. By continuing to fund wasteful experiments on animals, despite the agency's knowledge since at least 2013 that mouse-sepsis experiments do not replicate human sepsis but rather a separate condition and the abundant scientific evidence that the problems translating mouse sepsis to human sepsis also apply to other species used in sepsis experimentation, the NIH causes PETA to spend additional resources monitoring, documenting, analyzing, and addressing the government's expenditures of federal funding on animal-sepsis experiments and advocating that the agency adopt a funding paradigm relevant to human sepsis and consistent with its funding authority.

25. The NIH's funding of animal-sepsis experiments also causes PETA to spend additional resources educating the public about the futility of such experiments and about the availability and superiority of human-relevant, non-animal research approaches. Indeed, the NIH's actions create the misperception among the public that such experiments must be worthwhile for human health and a beneficial, justified use of taxpayer resources.

26. As a result of the NIH's unlawful actions and disregard of its own knowledge of the deficiencies of animal-sepsis experiments, PETA must divert resources away from other animal-protection projects in order to devote these resources to educating the public about and advocating for the cessation of wasteful, ineffective animal-sepsis experiments and for the funding of human-relevant sepsis research.

27. If it prevails in this lawsuit, PETA will no longer have to expend as many resources addressing the NIH's failure to comply with its funding authority, monitoring painful and futile animal-sepsis experiments receiving federal funding, writing the NIH regarding its funding of animal-sepsis experiments, and educating the public about these experiments. Those resources would then be directed to other PETA projects in furtherance of PETA's overall mission.

**Defendants**

28. Defendant HHS includes the NIH among its component agencies. The role of HHS within our nation's government is to enhance and protect human health. Accordingly, Congress has authorized funding of research toward the improvement of human health. HHS performs those duties primarily through the NIH, which has its headquarters in Bethesda, Maryland.

29. Defendant the NIH is a component of HHS and is the nation's largest funder of medical research. NIH makes decisions on whether to fund particular research grants, including

the grants at issue here, and has a duty to conduct scientific review before funding any grant in conformance with statutory and regulatory provisions.

30. Defendant Xavier Becerra is the Secretary of HHS. In that capacity, Secretary Becerra has a duty to coordinate research for the treatment, control, and prevention of human impairments. In performing that duty, Secretary Becerra is authorized to provide federal funding for such research.

31. Defendant Dr. Francis Collins is the Director of the NIH. Secretary Becerra's duties to fund research for the improvement of human health are carried out through Director Collins, who is responsible for setting NIH's policy and overseeing its funding priorities and decisions.

## STATUTORY AND REGULATORY FRAMEWORK

### I. The NIH's Actions Are Subject to the APA.

32. Pursuant to the APA, a reviewing court "shall . . . hold unlawful" agency actions that are arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law, 5 U.S.C. § 706(2)(A), or "in excess of statutory . . . authority, or limitations," *id.* § 706(2)(C).

33. "[A]gency action" includes "the whole or a part of an agency . . . relief . . . ." *Id.* § 551(13). "[R]elief" includes "the whole or a part of an agency--(A) grant of money . . . ." *Id.* § 551(11).

### II. The Public Health Service Act Authorizes Funding of Research for the Benefit of Human Health and Emphasizes Alternatives to the Use of Animals.

34. Under the Public Health Service Act, Congress directed the Secretary of HHS to carry out duties "relating to the causes, diagnosis, treatment, control, and prevention of physical and mental diseases and impairments of man." 42 U.S.C. § 241(a).

35. The Secretary of HHS acts through the Director of the NIH to undertake such duties. *Id.* § 282(b).

36. To fulfill that purpose, Congress directed that the Secretary of HHS, acting through the Director of the NIH, "shall by regulation require" that grant applications for NIH-supported research undergo "appropriate technical and scientific peer review." *Id.* § 289a(a)(1).

37. Likewise, to fulfill the purpose of improving human health, the Director of the NIH "shall ensure that research conducted or supported by" the NIH is subject to such peer review and that it is subsequently reviewed by an NIH advisory council prior to approval for funding. *Id.* § 282(b)(9).

38. Congress has also directed the NIH to support research that does not use animals and that reduces the number of animals used and the pain and distress produced in animals used in experimentation. *Id.* § 283e(a)(1)(A)-(C).

39. Thus, federal law mandates that expenditures of federal funds on NIH-supported research be for the benefit of *human* health and that the NIH support research that does not use animals and that reduces the number of animals used in experimentation and the pain and distress that experiments produce in animals.

## III. The NIH Must Conduct Technical and Scientific Review of Proposed Research.

40. Before proposed research receives NIH funding, Congress requires that it undergo "appropriate technical and scientific peer review," *id.* § 289a(a)(1), and review by an NIH advisory council, *id.* § 282(b)(9); *see also id.* § 289a-1 (requiring that proposals for NIH-supported research undergo technical and scientific peer review and review by advisory council prior to approval for funding).

41. In determining the scientific merit of an application, the NIH "shall assess the overall impact that the project could have on the research field involved." 42 C.F.R. § 52h.8.

42. In undertaking peer review, the NIH is required to consider, "among other pertinent factors . . . the adequacy of the approach and methodology proposed to carry out the research," "[t]he innovativeness and originality of the proposed research," and "[t]he adequacy of the proposed protection for . . . animals . . . to the extent they may be adversely affected by the project proposed in the application." *Id.* § 52h.8.

43. In describing its scoring criteria for assessing a grant proposal's scientific and technical merit, the NIH has elaborated on the requirement that the approach and methodology of a proposal be adequate:

> Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

NIH, Understanding Funding Opportunity Announcements: PA-18-345 16, *available at* https://grants.nih.gov/grants/Annotated_FOA.pdf.

44. Likewise, the NIH has elaborated on the innovation criterion:

> Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies,

> instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?
>
> Does the design/research plan include innovative elements, as appropriate, that enhance its sensitivity, potential for information or potential to advance scientific knowledge or clinical practice?

*Id.*

45. The NIH has also explained that in evaluating the use of live vertebrate animals as part of its assessment of scientific and technical merit, the committee will consider the following factors:

> 1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; 2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; 3) adequacy of veterinary care; 4) procedures for limiting discomfort, distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices; and 5) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia.

*Id.* at 18.

46. In addition to a funding application's scientific merit, the Secretary's evaluation of an application "shall take into account" both the significance and the feasibility of the project and "the likelihood of its producing meaningful results." 42 C.F.R. § 52.5(a).

## FACTS GIVING RISE TO PLAINTIFF'S CLAIMS

### I. Sepsis is a life-threatening condition for which experiments on animals have yielded no treatment for humans.

#### A. The Nature of Sepsis

47. "Sepsis is the body's extreme response to an infection." Sepsis, Centers for Disease Control and Prevention, https://www.cdc.gov/sepsis/what-is-sepsis.html.

48. In a typical year, sepsis afflicts at least 1.7 million adults in the United States, including one in three patients who die in a hospital, and kills nearly 270,000 Americans. *Id.*

49. Even when it does not cause death, sepsis can cause tissue damage and organ failure in some patients and, in others, excruciating pain.

#### B. The NIH's Authorization to Conduct Research for Human Health

50. The NIH is an agency of the Public Health Service within HHS. It is authorized by Congress to fund research for the benefit of human health.

51. The NIH describes itself as "the steward of medical and behavioral research for the Nation." NIH Grants Policy Statement I-42, Apr. 2021, *available at* https://grants.nih.gov/grants/policy/nihgps/nihgps.pdf. Such stewardship means that the NIH "is responsible to Congress and the U.S. taxpayer for carrying out its mission in a manner that not only facilitates research but does so cost-effectively and in compliance with applicable rules and regulations." *Id.*

52. Indeed, there is a longstanding federal directive for agencies to use public funds efficiently. *See, e.g.*, 31 U.S.C. § 712; Exec. Order No. 13, 450, 72 Fed. Reg. 64519 (Nov. 13, 2007).

### C. The NIH's Funding of Animal Experiments That Lack Relevance for Human Health

53. Notwithstanding its statutory directive to fund research to address impairments of humans, the NIH has funded animal-sepsis experiments that lack relevance to human sepsis since at least 1985.

54. Such experiments have cost taxpayers hundreds of millions of dollars.

55. Animal-sepsis experiments on mice and other animals inherently cause extreme pain. Cecal ligation puncture (hereinafter "CLP"), one method of introducing sepsis to animals in experiments, involves cutting open an animal's abdomen, puncturing their intestines with a needle so that bacteria will leak out, and then closing the perforated intestines back into the abdominal cavity. The animals then endure widespread pain, with the worst symptoms in the abdomen, and eventually become so sick that they are unable to move. They experience fever, chills, diarrhea, difficulty breathing, lethargy, disorientation, shock, multiple-organ failure, and, eventually, death—commonly after first suffering for one to two weeks. Another commonly used mouse model involves injecting a toxin to induce inflammation.

56. Sepsis can cause the animals used in experiments to become highly debilitated and have difficulty eating, drinking, moving around, and maintaining body temperature.

57. Decades of this degree of pain and suffering by hundreds of thousands of animals have not yielded any treatment for human sepsis. And the pain inherent in animal-sepsis experiments itself limits the experiments' translatability—their application to sepsis in humans. Pain and distress can impair the overall function of the immune system, affect disease progression, and confound the results of experiments.

58. For at least eighteen years, researchers have documented that sepsis induced in other species does not recapitulate sepsis in humans and have recognized the failure of animal-sepsis experiments to result in treatment for human clinical sepsis.

59. As researchers have repeatedly acknowledged, there are inherent, fundamental, immutable physiological differences between humans and the animals used in sepsis experiments. For example, baboons, rats, and mice are much less sensitive to bacterial toxins than humans are.

### D. NIH-funded 2013 Study That Confirms Animal Sepsis Experiments Are Not Relevant to Human Health

60. In 2013, the results were published of a landmark ten-year study involving the collaboration of 39 researchers from institutions across North America, as well as international experts. The researchers compared data obtained from hundreds of human clinical patients with results from experiments on mice to demonstrate that, when it comes to serious inflammatory conditions such as sepsis, burns, and trauma, mice have determinative differences from humans. The researchers pointed out that, as of February 11, 2013, "there ha[d] been nearly 150 clinical trials testing candidate agents intended to block the inflammatory response in critically ill patients, and every one of these trials failed." Junhee Seok et al., *Genomic responses in mouse models poorly mimic human inflammatory diseases*, 110(9) PNAS 3507, 3507-12 (2013). Since this publication, there have been hundreds more such clinical trials, yet there has been no significant improvement in patient care.

61. The researchers set forth comprehensive data showing why results from mouse-sepsis experiments do not reflect human disease, demonstrating why the contrary cannot be assumed.

62. Following the publication of the study, NIH Director Dr. Francis Collins wrote, "No wonder drugs designed for the mice failed in humans: they were, in fact, treating different

conditions!" Francis Collins, Of Mice, Men, and Medicine, https://directorsblog.nih.gov/2013/02/19/of-mice-men-and-medicine/#mo (Feb. 19, 2013). The NIH cannot assume that sepsis experiments on mice and other species reflect human sepsis in any meaningful fashion; the agency knows that they do not.

63. Collins acknowledged that "150 drugs that successfully treated this condition in mice later failed in human clinical trials—a heartbreaking loss of decades of research and billions of dollars." The NIH has not released an updated number of drugs that have successfully treated the condition in mice or other animals but failed in human clinical trials.

64. He further stated, "The new study provides more reason to develop better and more sophisticated models of human disease."

### E. The NIH's Continued Funding of Animal Experiments Notwithstanding Their Lack of Relevance

65. Since Collins posted his blog, the NIH has approved grants that provide federal funding of hundreds of millions of dollars for sepsis experiments on mice and other animals.

66. Mice are the most commonly used species in sepsis experimentation—not because they have relevance for human sepsis, but because they are convenient; they are small and easy to breed and maintain. Additionally, mice continue to be used simply because they have been used so frequently in the past, resulting in an accumulation of data to which new experiments are compared. Other animals used in sepsis experiments are no more effective at replicating the human condition.

67. In 2019, a working group on sepsis at NIH acknowledged that the "utility" of rodents to develop "new therapies or diagnostics faces substantial doubt in the broader scientific community." National Advisory General Medical Sciences Council Working Group on Sepsis Final Report 8 (2019), *available at* https://www.nigms.nih.gov/News/reports/Documents/nagmsc-

working-group-on-sepsis-final-report.pdf. In fact, at least fifteen peer-reviewed publications over the past eighteen years have described how sepsis in humans fundamentally differs from sepsis in other animals. Many have specifically discussed how the use of mice has contributed to the lack of progress to develop treatments in this area. The NIH working group found the relevance of experiments on mice to be "in question, raising concerns that current 'best practice' may not be a reliable tool in making translatable discoveries." *Id.* at 10. Indeed, in discussing CLP—considered the "gold standard" for studying sepsis induction in animals despite decades of its failure to apply to sepsis in humans—the working group even admitted that there is "doubt [concerning] its utility in studying the majority of human experience." *Id.* at 7.

**F. Fundamental Differences between Sepsis in Animals and in Humans**

68. Aside from inherent species differences, there are significant disparities between the introduction of, circumstances surrounding, and management of animal sepsis and the actual clinical situation for humans, as well as fundamental issues with experimental design that impair the internal validity of animal-sepsis studies—the scientific robustness of their design, performance, and analysis. Human septic patients are usually receiving fluids and organ support therapies or technologies; animals in experiments are not, which makes it difficult to extrapolate results of experiments to human patients. Most animals in sepsis experiments are young and healthy, which differs from the typical human sepsis patient. Sepsis has acute onset for animals used in experiments, but its onset in humans varies and can be difficult to gauge; there is a controlled artificiality in animal sepsis models that is not applicable or salient to the human experience. Animals in experiments receive intervention before or during the early stages of sepsis, but human patients already have apparent organ damage when starting treatment.

Experimenters can choose an appropriate antibiotic for animals because they have introduced a particular bacterial strain, but human patients have often unknown bacteria or mixed infections.

69. Poor internal validity means the data generated will not be reproducible, a critical aspect of the scientific process that speaks to the robustness of a finding. Animal-sepsis experiments are not only unsound when applied to other situations and species, but also when held against themselves.

**G. Promising Non-Animal Sepsis Studies**

70. Contrary to the animal-sepsis experiments, which do not pertain to human sepsis, there is human-relevant sepsis research that does not involve persistently flawed experimentation on other species. For example, groundbreaking work in the field of sepsis research is being done to better understand the condition by studying phenotypes, endotypes, and proteomic responses in human sepsis patients. Such work is in the early stages but is far more promising than ineffectual animal models for therapeutic development.

**H. The NIH's Flawed Paradigm of Funding Animal Sepsis Experiments**

71. Despite the NIH's explicit acknowledgment more than eight years ago that drugs developed on mice do not work on humans because they are not treating human sepsis and the copious scientific evidence regarding the inefficacy of animal-sepsis experiments for treating human patients, the NIH remains entrenched in funding a flawed paradigm and perpetuating research that has failed for decades. The agency continues to approve grants for animal-sepsis experiments—including those that do not even attempt to correct well-documented shortcomings—methodological limitations in experimental design that have been extensively critiqued within the scientific community; its actions not only fly in the face of good science but also contravene the agency's statutory authority and funding criteria.

## I. PETA's Unheeded Request to the NIH to Cease Funding Animal-Sepsis Experiments

72. Considering the well-documented flaws in sepsis research on animals and the gravity of the harm sepsis presents to millions of Americans, PETA wrote to the NIH on October 23, 2019, to request that the agency cease funding animal-sepsis experiments and steward federal support for the study of human-relevant methods of treating human sepsis.

73. On November 14, 2019, the agency responded, reiterating its position that there may be something the mouse can still "teach us" and taking PETA's materials "under further advisement."

74. This Complaint describes five grants recently funded by the NIH as illustrative but challenges the NIH's funding of animal-sepsis experiments since October 23, 2019. When the NIH awarded these grants, the agency had ample evidence that it was funding experiments that it has known for years do not relate to human health—its controlling criterion imposed by Congress. Further, there cannot be adequate protection for animals or justification for their use in animal-sepsis experiments when they do not experience human sepsis and have not led to one pharmacological treatment for human sepsis over the past three decades.

75. The NIH's actions in funding these and further animal-sepsis experiments are arbitrary, capricious, an abuse of discretion, not in accordance with law, and in excess of statutory jurisdiction, authority, or limitations within the meaning of the APA, 5 U.S.C. § 706(2)(A), (C).

76. The NIH follows a policy, pattern, and practice that—regardless of all data to the contrary—animal-sepsis experiments are still related in some distant way to human sepsis, rooting itself in speculative aspirations that decades of research and billions of dollars have shown to be unsupportable. This approach is not a reasonable or lawful interpretation of the mandate that the NIH support research that relates to human impairments, that any use of animals be justified, and

that the NIH support research that reduces the use of animals in experiments. As a result, the NIH's position and the resulting funding decisions are arbitrary, capricious, an abuse of discretion, not in accordance with law, and in excess of statutory jurisdiction, authority, or limitations within the meaning of the APA, 5 U.S.C. § 706(2)(A), (C).

## II. Recently Funded Animal-Sepsis Grants

### A. Project Number R21NS121504

77. On February 3, 2021, the NIH awarded $425,028 to The University of Pittsburgh for a grant to induce sepsis in mice via CLP and study a specific membrane channel.

78. There is no indication that the mice will receive antibiotics or will receive respiratory or blood pressure support once sepsis sets in, a major difference from the human clinical situation that has been identified as negating the results of treatments developed under such conditions. Further, the mice to be used will be young and otherwise healthy—other factors that are known to differ markedly from typical human sepsis patients and to undermine the results of research purportedly for their benefit.

79. Between September 2016 and February 2017, PETA conducted an eyewitness investigation of animal-sepsis experiments at the University of Pittsburgh, where an experimenter used the very same method proposed in this grant—CLP—to perforate mice's intestines and let bacteria leak into their stomachs. According to a University of Pittsburgh veterinarian, the mice used were "falling over dead" in their cages. Four years later, and eight years since the NIH acknowledged that drugs developed on mice do not treat human sepsis, the NIH is continuing to fund the study of animal sepsis at the University of Pittsburgh.

### B. Project Number 1R01AI152044-01A1

80. On January 27, 2020, the NIH awarded $405,956 to The University of Pittsburgh for its plans to induce sepsis in mice. The university will use CLP and will also inject the toxin

lipopolysaccharide (hereinafter "LPS") to cause peritonitis—inflammation of an abdominal membrane—in mice and inject the bacterium *E. coli* into the abdomen of mice.

81. LPS induces severe septic shock, which is a potentially fatal condition resulting from uncontrolled sepsis; it is a widespread pathophysiological process that causes dangerously low blood pressure and organ failure.

82. Injecting an animal with a bacterial toxin is a particularly inapplicable model for human sepsis, as members of the research community described more than ten years ago. It is perhaps not even an accurate model for sepsis in mice. Indeed, LPS sepsis "models" do not model sepsis at all. Mice are more resistant to a bacterial toxin than humans are. In addition, the bacterial-infection model of experimentation is not a true septic model and fails to replicate many significant aspects of clinical sepsis.

83. The experimenters will not employ respiratory (e.g., a ventilator) support for the mice, and will use young adult, apparently healthy mice.

**C. Project Number R21AI152050**

84. On June 2, 2020, the NIH awarded $233,016 to Texas A&M Agrilife Research to induce sepsis in mice via CLP.

85. Again, the experimenter will not provide the mice with respiratory support, though the lack of such support has been identified as negating the results of treatments developed under such circumstances, or with antibiotics, another major deviation from the human clinical situation that has been identified as one factor in the ongoing failure of experiments such as these to translate to the human clinical situation. The experimenter also uses young mice.

86. The experimenter's justification for using mice is that mice are regularly used for the techniques to be employed—which simply perpetuates the use of flawed models because those models are commonly used—and invokes the "gold standard" description of the CLP mouse

model. It appears that, in performing a literature search for alternatives to experiments on animals, as required by law, the grantee did not include CLP or sepsis models among the search terms. This apparent omission highlights the automatic reliance that NIH-funded research places on procedures whose flaws in treating human health concerns have been documented at length.

**D. Project Number R21AI147168**

87. On January 27, 2020, the NIH awarded $247,500 to Boston University Medical Campus to induce sepsis in mice via CLP.

88. In the description of their project, the experimenters acknowledge, "[F]lawed murine models have not produced effective clinical therapies." Nonetheless, the NIH granted them nearly a quarter of a million dollars to experiment on mice.

89. The experimenters likewise use healthy, young mice and do not use respiratory support.

90. Some of the mice will receive a combination of vitamin C, hydrocortisone, and thiamine, and the experimenters will measure certain markers of inflammation and sepsis-related organ dysfunction. This therapy was found in 2017 as a result of a study of sepsis in humans.

91. The NIH thus approved a proposal that seeks to take a therapy that is able to be and has been tested in humans with sepsis and administer it to mice, who do not experience human sepsis, at the cost of hundreds of thousands of dollars for one award year. Further, it uses CLP, deficiencies of which are long documented within the research community.

**E. Project Number R21AI150723**

92. On January 27, 2020, the NIH awarded $191,719 to Augusta University to induce sepsis in rats and mice via LPS, with CLP as a possible alternate approach.

93. The experimenters refer to "the gold-standard endotoxin (lipopolysaccharide) model of endotoxic shock in rats," ignoring that a standard that has been regarded as the best of failed models is still a failed model.

94. The experimenters are not providing respiratory support and have not stated whether the animals being used are young and healthy.

95. In all of the above, the NIH approved grants that maintain the same paradigm it conceded to be fruitless for human sepsis patients in 2013 and that did not even deviate from the same flawed induction methods and experimental design that sepsis researchers have long and repeatedly identified as lacking relevance to human sepsis and as undermining the results of experiments employing them. Besides the longstanding shortcomings in experimental design that hinder research that is meaningful for human health, animal-sepsis studies are inherently flawed for the purpose of treating human sepsis. If the NIH were an agency tasked with providing funding for the improvement of murine health, its actions might fall within its mandate. However, as the agency tasked with stewarding federal resources for the benefit of *human* health and deploying those resources only after meaningful examination of a proposed study's scientific merit within particular criteria, including the reduction of and justification for the use of animals, the NIH's actions are arbitrary, capricious, an abuse of discretion, and not in accordance with law.

## FIRST CAUSE OF ACTION

96. The NIH's approvals of grants to conduct sepsis experiments on animals since October 23, 2019, represent final agency actions that are reviewable under the APA because they constitute the agency's grant of money and represent the culmination of the agency's decision-making process. The agency's approvals of the grants are arbitrary, capricious, an abuse of discretion, and not in accordance with law, within the meaning of the APA, 5 U.S.C. § 706(2)(A),

and exceed the NIH's statutory jurisdiction, authority, or limitations within the meaning of 5 U.S.C. § 706(2)(C), because the agency's actions run counter to the evidence surrounding animal-sepsis experimentation, lack a rational connection to the data and the agency's own concessions regarding its failings, and are not a reasonable interpretation of the statutory authority to fund research for human impairments and the criteria for such funding.

97. The NIH's unlawful actions injure Plaintiff in the manner specified in ¶¶ 1-95.

## SECOND CAUSE OF ACTION

98. The NIH's ongoing policy, pattern and practice, as characterized in its November 14, 2019, response to PETA's report, of approving grants for inherently flawed animal-sepsis studies because, after decades, mouse-sepsis experiments might teach something about human sepsis through the condition's very differences from human sepsis, is arbitrary, capricious, an abuse of discretion, and not in accordance with law, within the meaning of the APA, 5 U.S.C. § 706(2)(A), and exceeds the NIH's statutory jurisdiction, authority, or limitations within the meaning of 5 U.S.C. § 706(2)(C). This policy, pattern, and practice is contrary to the evidence and the agency's own admissions and is not a reasonable interpretation of the statutory authority to fund research for human impairments and the criteria for such funding.

99. The NIH's unlawful actions injure Plaintiff in the manner specified in ¶¶ 1-95.

## PRAYER FOR RELIEF

**WHEREFORE**, Plaintiff respectfully requests that the Court:

1. Declare that Defendants acted arbitrarily, capriciously, and not in accordance with law; abused their discretion; and exceeded their statutory jurisdiction, authority, and limitations in awarding grants for sepsis experimentation on animals when the agency has long known such experiments fail to translate to human sepsis;

2. Enjoin Defendants from awarding grants for sepsis experiments on animals;

3. Declare that Defendants' policy, pattern and practice of funding animal-sepsis experiments, contrary to the agency's understanding of their failure to translate to human sepsis and the controlling mandate and criteria for NIH-supported research, is arbitrary and capricious, not in accordance with law, an abuse of discretion, and in excess of Defendants' statutory jurisdiction, authority, and limitations;

4. Award Plaintiff its reasonable attorneys' fees and costs; and

5. Grant such other and further relief as the Court may deem just and proper.

Dated September 20, 2021

Respectfully submitted,

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