IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

CENTER FOR RESPONSIBLE SCIENCE,
Post Office Box 443
Pacific Palisades, CA 90272

HAL GARCIA-SMITH,
2122 8th Ave. N., #201
Seattle, WA 98109

JOHN TESSMER,
5644 Soledad Road
La Jolla, CA 92037

and

MICHAEL VOKHGELT,
73 S. Ardmore Road
Columbus, OH 43209,

Plaintiffs,

v.

DR. SCOTT GOTTLIEB, in his official capacity as the Commissioner of the Food and Drug Administration,
10903 New Hampshire Avenue
Silver Spring, MD 20993,

Defendant.

Docket No.

COMPLAINT

Plaintiffs Center for Responsible Science (when abbreviated, "CRS"), Hal Garcia-Smith, John Tessmer, and Michael Vokhgelt, by and through their counsel, Alan C. Milstein of Sherman, Silverstein, Kohl, Rose & Podolsky, P.A., bring this Complaint against Defendant Dr. Scott Gottlieb, in his official capacity as the Commissioner of the Food and Drug Administration ("FDA"), as well as his agents and successors in office, and hereby say, state, and aver as follows:

THE PARTIES

The Center for Responsible Science:

1. The Center for Responsible Science is a non-profit group of scientific, medical, regulatory, business, and legal professionals who promote advances in regulatory science.

2. Such advances include the use of modern, predictive preclinical test methods in an effort to streamline drug and device development and bring safer, more effective products to patients more quickly at less cost.

3. Through collaboration with scientific, educational, legal, health care, patient advocacy, and biotech communities, CRS advocates for better results for patients.

4. CRS moves product development forward by bringing policy up to date with existing science, and paving the way for use of emerging technologies that will better protect the public. CRS monitors serious adverse events, including treatment-related deaths in clinical trials.

5. CRS works directly with the scientific community to stay up to date on the latest advances in preclinical test methods that could better protect clinical trial participants.

6. CRS has been invited to make, and was the first non-member to make, a research presentation to a private meeting of the Interagency Coordinating Committed on the Validation of Alternative Methods (ICCVAM). ICCVAM is a permanent committee of the National Institute of Environmental Health Sciences (NIEHS) under the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM). ICCVAM is composed of representatives from sixteen U.S. federal regulatory and research agencies that require, use, generate, or disseminate toxicological and safety testing information.

7. CRS attends the annual ICCVAM Public Forum and submits extensive written comments, as well as provides oral comments during the meeting. CRS also attends the annual

meeting of the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM). Dr. Neil Wilcox, former FDA Senior Science Policy Officer, Office of Science, Office of the Commissioner and Science Policy Analyst, and CRS President, provides oral comments at the annual meeting. SACATM is a federally chartered advisory committee established by the ICCVAM Authorization Act of 2000.

8. CRS has published articles in the Food and Drug Law Institute Policy Forum and scientific journals.

Hal Garcia-Smith:

9. Plaintiff Hal Garcia-Smith has worked in the field of HIV/AIDS since 1985.

10. He currently works as a Disease Intervention Specialist for the King County Public Health STD clinic at Harborview Medical Center in Seattle, Washington.

11. Mr. Garcia-Smith previously participated in a Phase III AIDSVAX B/B clinical trial to determine the safety and efficacy of AIDSVAX in preventing HIV infection in people who are at risk of being infected.

12. The approximately 5,000 volunteer participants, including Mr. Garcia-Smith, consisted of HIV-negative men who have sex with men (MSM), and HIV-negative women who have HIV-infected sexual partners or are part of a population at higher risk of HIV infection.

13. As a gay man, Mr. Garcia-Smith had seen the impact of HIV/AIDS on his community, and participated in the clinical trial for altruistic reasons.

14. Mr. Garcia-Smith was told it was safe, and, based upon his review of the representations within the informed consent document, was not concerned about the risks associated with participating in the trial.

15. Mr. Garcia-Smith would like to participate in clinical trials in the future for altruistic reasons, including helping those in his community.

16. Mr. Garcia-Smith, however, believes researchers should not ask him and others to risk their lives and health unless those researchers provide the disclosures regarding animal testing set forth in the requested regulations (discussed below).

John Tessmer:

17. Plaintiff John Tessmer is a professional actor who lives in San Diego, California.

18. He has been an actor for approximately thirty years.

19. Mr. Tessmer received his B.A. in English from Yale University, and his M.F.A. in Theatre/Acting from the University of Wisconsin-Milwaukee.

20. Through the years, Mr. Tessmer has found it necessary to supplement his income from acting with income from other jobs, and a number of clinical trials.

21. In 2001, due to his financial needs, Mr. Tessmer began participating in Phase I clinical trials, and continued participating in clinical trials thereafter.

22. It is Mr. Tessmer's routine and practice, prior to enrolling in any given clinical trial, to thoroughly review the informed consent document and other documentation associated with the trial.

23. If Mr. Tessmer feels, based upon his review of those documents, that there is a real risk associated with participation, he declines to participate.

24. His financial situation is such that he will need to participate in clinical trials in the future, in order to supplement his income, yet he is often now unable to participate in trials because he now knows that he is not usually given a complete disclosure of the risks.

Michael Vokhgelt:

25. Plaintiff Michael Vokhgelt is the father of the late Max Vokhgelt, who passed away in May 2016 at the age of twenty-four.

26. Max participated in a Phase II clinical trial of chimeric antigen receptor T-Cell

(CAR-T) therapy, an experimental cancer therapy that uses a patient's T cells that are changed in the laboratory so they will attack cancer cells, which therapy was developed by Juno Therapeutics ("Juno").

27. Animal studies purported to demonstrate the safety of the therapy such that the trial could proceed to the human subjects stage.

28. In May 2016, Max died from cerebral edema as the result of his participation in the trial.

29. On June 4, 2016, one week after Max's death, Juno announced in a press release "that encouraging clinical data from JCAR015, a chimeric antigen receptor (CAR) T cell product candidate, support its strategic approach towards the commercialization of its first CAR T therapy." Juno did not announce Max's death at that time.

30. Shortly thereafter, Hans E. Bishop, Juno's CEO, sold over $8,600,000 worth of shares.

31. On June 7, 2016, Juno submitted an 8-K SEC filing with an updated corporate report. Juno did not include information on Max's death in the report.

32. Max's death was not reported until July 13, 2016, after two more participants died from cerebral edema.

33. Around this time, FDA issued a "clinical hold"[1] in connection with the trial, but lifted the hold just five days later, based on Juno's assertion that the deaths were caused by fludarabine, the chemotherapy preconditioning agent, in combination with the CAR-T therapy. Studies show the median length of a clinical hold is eight months.

34. Juno resumed the trial without fludarabine.

[1] "A clinical hold is an order issued by FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation." See 21 C.F.R. § 312.42.

35. Two more clinical trial participants died from cerebral edema in November 2016.

36. Neither Max Vokhgelt nor his father Michael was informed, prior to Max's participation in the clinical trial, that animal testing does not always predict toxicities in humans.

Food and Drug Administration:

37. FDA is a division of the Department of Health and Human Services ("DHHS").

38. Defendant Dr. Scott Gottlieb is presently the Commissioner of FDA.

39. Dr. Gottlieb is being sued in his official capacity as the Commissioner of FDA.

40. By virtue of this action, the Plaintiffs are bringing suit against Dr. Gottlieb, in his official capacity as Commissioner of FDA, as well as his agents and successors in office.

SUBJECT MATTER JURISDICTION AND VENUE

41. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. § 1331, which provides that "[t]he district courts shall have original jurisdiction of all civil actions arising under the Constitution, laws, or treaties of the United States," because this civil action arises under the Constitution and laws of the United States.

42. Venue is proper in this judicial district pursuant to 28 U.S.C. § 1391, including without limitation § 1391(d), as the Defendant is deemed to reside within this district for purposes of this action, and a substantial part of the events or omissions giving rise to the claim occurred within this district.

43. According to FDA's web site (last visited July 6, 2017):

> The Food and Drug Administration's mission of protecting and promoting public health is not held to one region. As such, we have offices and staff in the Washington, D.C. area as well as across the United States (field locations) and, most recently, at international locations including China, India, Europe, the Middle East, and Latin America.
>
> FDA headquarters facilities are located in Montgomery and Prince Georges Counties in Maryland. Many FDA employees are

consolidated at the White Oak Campus located in Silver Spring, MD. Remaining headquarters employees are housed in numerous additional buildings located across the Washington, D.C. area.

44. Moreover, FDA is a division of DHHS, which is headquartered at 200 Independence Avenue S.W., Washington, D.C. 20201.

FACTS COMMON TO ALL COUNTS

45. In the United States of America, as elsewhere, investigational drugs are tested in clinical trials to determine whether or not they should be approved for wider use within the general population.

46. Under the current paradigm of drug development, animal models are considered to be the "gold standard" during preclinical testing.

47. Thus, prior to the testing of a drug in a human subject experiment, that drug is tested for safety (as well as for efficacy) in laboratory animals.

48. Due to inter-species differences in the pharmacodynamics (effects) and pharmacokinetics (movement) of drugs, however, data from preclinical animal testing often does not translate to expected results in human clinical trials.

49. Indeed, many new experimental drugs have species-dependent effects that traditional animal tests are unable to predict.

50. Thus, animal testing can be considered a poor predictor of pharmacodynamics and pharmacokinetics for humans.

51. Indeed, as many as ninety-five percent of all drugs that successfully passed preclinical animal testing fail during human clinical trials. See https://grants.nih.gov/grants/guide/notice-files/NOT-TR-16-002.html.

52. FDA has been delegated the duty to promulgate regulations governing drug trials.

53. Individuals who are considering the possibility of participating as human subjects

in clinical drug trials rely upon FDA regulations to ensure that the sponsors of clinical trials, most often drug companies, provide adequate information to enable potential subjects to make informed decisions regarding their participation in such research.

54. Over the past eighty years, ethical standards regarding human research have significantly evolved, reflecting the view that increased levels of protection must be afforded to human research subjects.

55. FDA's disclosure regulations designed to protect human research subjects, however, are now decades old, and require revision.

56. Current FDA regulations governing drug trials require the disclosure of "a description of any reasonably foreseeable risks and discomforts to the subject." See 21 C.F.R. § 50.25(a)(2).

57. Because the regulations do not further specify the content of such disclosure, however, drug sponsors are able to avoid making the specific disclosure that preclinical animal testing may not predict the degree of risk to which the human subjects participating in the trial will be subjected.

58. Moreover, studies have demonstrated a "therapeutic misconception" whereby many drug trial participants are not only ignorant of the potential risks of participating in a clinical trial, they actually believe they will receive a personal benefit from the trial; in reality, for the vast majority of Phase I trials, no therapeutic benefit is expected, and benefits are unlikely in Phase II and III trials.

59. Since the current drug development paradigm relies heavily on preclinical animal data, however, human subjects participating in drug trials are subject to unquantifiable risk.

60. Because risk exists that cannot be eliminated, FDA regulations must mandate that

prospective clinical trial participants receive adequate disclosure and warnings.

61. Indeed, human clinical trials deal with the unknown, and it is therefore medically and scientifically important to give participants all information necessary to aid in making the decision whether to participate.

62. In light of the convincing evidence that human subjects are currently participating in clinical trials without a full understanding of attendant risks, there is no public policy justification for FDA's refusing to act.

63. The current applicable FDA regulation is found at 21 C.F.R. § 50.25, and reads in pertinent part as follows:

> § 50.25 Elements of Informed Consent.
>
> (a) Basic elements of informed consent. In seeking informed consent, the following information shall be provided to each subject:
>
> (1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
>
> (2) A description of any reasonably foreseeable risks or discomforts to the subject.
>
> (3) A description of any benefits to the subject or to others, which may reasonably be expected from the research.
>
> (4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
>
> (5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.
>
> (6) For research involving more than minimal risk, an explanation as to whether any compensation and an

> explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
>
> (7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
>
> (8) A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

64. FDA allows citizens to petition it to amend FDA regulations. See 21 C.F.R. § 10.25(a) ("An interested person may petition the Commissioner to issue, amend, or revoke a regulation or order, or to take or refrain from taking any other form of administrative action."); see also id. § 10.30.

65. On or around May 30, 2014, CRS submitted a citizen's petition ("Petition") to FDA that was co-signed by Mr. Tessmer and Mr. Garcia-Smith (collectively, "Petitioners").

66. A true and correct copy of the Petition, including the fifty-five exhibits attached thereto, is attached to this Complaint as Exhibit "A."

67. By virtue of the Petition, the Petitioners requested that FDA amend its disclosure regulations to ensure that human subjects entering into clinical drug trials receive sufficient information to enable them to provide true informed consent with regard to their participation in the trials. See generally Exhibit A.

68. Specifically, the Petitioners requested that FDA "add the following new Sections (9) – (11) to 21 C.F.R. § 50.25(a), providing a set of standard warnings in the informed consent document for every phase of clinical drug trials" (boldface in original):

> **(9) The drug you will be given has been tested in animals and by other laboratory methods to determine whether it is**

> **likely to be safe and effective in humans. The decision to allow testing of this drug on humans relies heavily on the presumption that animal tests predict human response. Due to differences between animals and humans, animal tests may not predict whether a drug is safe and/or effective for use in humans.**
>
> **(10) Some participants in clinical trials in which other investigative drugs were tested have died or have been seriously injured by the drug that was tested.**
>
> **(11) The drug you will be given may later prove to be either unsafe for humans or ineffective in treating the condition for which it is being tested. You should not assume the drug will treat a medical condition you may have, because a determination of efficacy in an animal study does not necessarily predict efficacy in humans.**

See Exhibit A, page 7 (boldface in original).

69. The Petitioners provided a detailed, heavily footnoted "Statement of Grounds" for their Petition and the amendment to the regulations requested therein.

70. The "Statement of Grounds" began with the following history.

71. After World War II, the Nuremberg Trials were conducted in part to prosecute Nazi physicians who performed research on prisoners in concentration camps.

72. These trials laid the foundation for the Nuremberg Code, a set of international ethical principles that investigators are expected to follow when conducting experiments involving human subjects.

73. Subsequent to the enactment of the Nuremberg Code, but prior to FDA's regulation of human subject research, doctors prescribed thalidomide to pregnant women in Europe. Thalidomide became an over-the-counter drug in West Germany in 1957. Shortly after the drug was sold in West Germany, between 5,000 and 7,000 infants were born with phocomelia (malformation of the limbs). Only 40% of these children survived. The FDA refused to approve thalidomide for marketing and distribution. However, the drug was

distributed in large quantities for testing purposes, after the American distributor and manufacturer Richardson-Merrell had applied for its approval in September 1960.

74. As a result, over 10,000 women from various countries gave birth to babies with deformed or missing limbs.

75. In 1962, the Kefauver-Harris Amendments to the Food, Drug, and Cosmetic Act added a requirement that investigators in the United States obtain informed consent from participants before administering an investigational drug.

76. In 1964, the World Medical Association met in Helsinki, Finland to write and adopt a declaration, which came to be known as the Declaration of Helsinki, describing ethical standards to guide biomedical research involving human subjects.

77. The declaration incorporated the principle of informed consent, meaning that each human research subject must be adequately informed of the aims of the research; the methods used to conduct the research; the anticipated benefits and potential hazards; the sources of funding and possible conflicts of interest; and the right to withdraw from the study.

78. Despite the existence of the Nuremberg Code, the Declaration of Helsinki, and the Kefauver-Harris Amendment, deplorable research misrepresentations continued.

79. A striking example was the infamous Tuskegee syphilis experiment, funded by the United States government, which lasted from 1932 to 1972.

80. 600 African-American men, approximately 400 of whom had syphilis, participated in the study.

81. The researchers misled the participants, failed to give them all the facts required for informed consent, and failed to provide adequate treatment for their disease.

82. Indeed, in the late 1940s, physicians began treating syphilis with penicillin, which

proved to be highly effective; the researchers, however, did not disclose to the subjects that a highly effective treatment was available, offer the treatment to the subjects, or give the subjects the choice of quitting the study.

83. In 1974, following a public outcry about the Tuskegee syphilis experiment, Congress passed the National Research Act, which established the National Commission for Protection of Human Subjects of Biomedical and Behavioral Research ("Commission").

84. In 1978, the Commission issued the Belmont Report, which outlined minimum requirements for ethical human subjects research.

85. Under the Belmont Report, human research subjects must enter into research voluntarily, and with adequate information, including the purpose of the research; the risks and anticipated benefits; alternatives; and the right to withdraw from the research.

86. Ultimately, responsibility for overseeing compliance with human research subjects was given to the Department of Health and Human Services ("DHHS"), under the Office for Human Research Protections ("OHRP").2

87. The OHRP issued revised federal regulations, which became known as the Common Rule, which aimed to eliminate confusion and promote uniformity among the federal departments or agencies that conduct, support, or regulate human subjects research. See 45 C.F.R. § 46.101, et seq.

88. Currently, DHHS regulates research involving human subjects conducted or supported by DHHS, and FDA regulates research involving human subjects for drug

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[2] As the Petition noted, institutional review boards overseeing research may require that additional information be given to human subjects, if the IRB determines that the information will meaningfully add to the protection of the subjects' rights and welfare. Further, other federal, state, and local laws and regulations can require disclosure of additional information beyond DHHS and FDA requirements. See, e.g., 21 C.F.R. § 50.25(d).

development and medical devices.

89. FDA did not adopt the Common Rule in its entirety, but adopted certain provisions of the Common Rule within FDA regulations meant to protect human research subjects in clinical trials.

90. The Petition's "Statement of Grounds" then discussed FDA's role in the stages of drug development, as follows.

91. Drug development starts with what is called the discovery phase, where compounds are both designed and synthesized.

92. Subsequently, preclinical testing begins, which includes testing compounds in vitro in cultured cells and in vivo in laboratory animals.

93. If investigators decide, based upon the preclinical data, that the drug is potentially beneficial and safe for use in humans, the drug sponsor submits an investigational new drug application ("IND") to FDA.

94. If FDA is satisfied that the data submitted within the IND shows the drug is reasonably safe for testing in humans, and an IRB approves protocols for a proposed human clinical trial, investigators may move forward with the trial.

95. A Phase I trial marks the introduction of an investigational new drug to human subjects.

96. Such trials generally consist of between twenty and eighty healthy volunteers, and attempt to determine the drug's proper dosing, pharmacokinetics, and side effects.

97. Assuming an absence of an unacceptable toxicity, Phase II trials follow.

98. During Phase II trials, investigators test between a few dozen and 300 patients, who have the medical condition the drug is intended to treat, to determine whether the drug is

effective for that condition.

99. If Phase II clinical trials demonstrate efficacy, and an absence of toxicity, investigators proceed to Phase III testing.

100. Phase III clinical trials seek to examine both safety and efficacy in between several hundred and several thousand subjects.

101. Ultimately, FDA analyzes the human data, and determines whether to approve the drug for use in the general population.

102. The "Statement of Grounds" then pointed out that existing informed consent regulations are inadequate in light of two significant changes that have occurred since they were enacted: (1) the science of drug development has progressed; and (2) ethical standards have evolved.

103. With regard to animal testing, researchers accept animal testing as a precursor to human testing because current regulations require it, and investigators are trained to believe that animal testing is the "gold standard."

104. Animal models, however, have never been scientifically validated for the purpose of testing drugs intended for humans.

105. One reason that animal models have never been scientifically validated is that the concept of scientific validation (demonstrating reproducibility, repeatability, and usefulness) did not exist at the time when animal models were developed.

106. In the absence of scientific validation, animal models are simply accepted on "good-faith that these studies are the best approach for protecting humans," with no proof that any particular animal model actually predicts human response.

107. There now exists compelling evidence demonstrating that animal models can be

poor predictors of human response.

108. Indeed, animal models have been shown to be problematic in screening drugs for humans, because the data often cannot be transposed to humans, due to among other things inter-species differences in drug pharmacodynamics and pharmacokinetics.

109. As a result, some unexpected and sometimes very serious outcomes occur in human clinical trials.

110. Indeed, the inability to assess and predict drug safety through animal testing in preclinical studies has led to repeated failures during clinical development, and "[t]he vast majority of drugs that enter into human trials never survive to licensure."

111. A 2007 systematic survey found that eighteen of twenty reviews published in peer-reviewed journals indicate animals are insufficiently predictive of human clinical or toxicological outcomes.

112. Similarly, a 2013 study showed limited concordance between treatment effects in animal experiments and subsequent clinical trials in humans.

113. A 2015 study analyzed data from non-human primates, which are considered the animals most likely to have the most human relevance, found that when no toxicity was found in the animal tests, these tests contributed very little to no evidential weight to the probability of lack of toxicity in humans.

114. These studies concluded that animal tests have essentially no ability to predict the absence of toxicity in humans. Investigational drugs proceed to testing in humans when no toxicity appears in animal testing, which creates a false sense of security and puts clinical trial participants at risk. While animal tests undoubtedly prevent some toxic drugs from reaching humans, they cannot predict safety for humans.

115. Another study found that only forty-six percent of visible human adverse reactions occurred in animals, making the predictive likelihood of adverse reactions akin to the results of a coin toss.

116. Critically, FDA itself has issued numerous statements acknowledging that reliance on animal models is inadequate, and results in high clinical failure rates.

117. For example, a 2006 FDA news release stated as follows (emphasis added): "Currently, nine out of ten experimental drugs fail in clinical studies because we cannot accurately predict how they will behave in people based on laboratory and animal studies."

118. In 2004, as part of the Critical Path Initiative to drive innovation in drug development, FDA reported that ninety-two out of 100 drugs that successfully pass pre-clinical animal testing subsequently fail during clinical trials when the drug is tested in humans.

119. By way of background, official FDA guidance documents for cellular and gene therapies acknowledge that traditional animal tests may not be informative with regard to human toxicity due to species-specificity and other issues:

> In addition, the preclinical data generated for CGT products may not always be as informative as for small molecule pharmaceuticals, particularly since it usually is not feasible to conduct traditional preclinical pharmacokinetic (PK) studies with CGT products."[3]
>
> However, traditional PK study designs are generally not feasible for CGT products; thus, such data are not available to guide clinical trial design. Due to various issues, such as species specificity and immunogenicity, extrapolation from a CGT product dose administered in animals to a clinical dose can be less reliable than the customary allometric scaling typically used for small-molecule pharmaceuticals."[4]

120. Also, by way of background, a 2016 Scientific Advisory Committee on Alternative

[3] Considerations for the Design of Early-Phase Clinical Trials of Cellular and Gene Therapy Products, Guidance for Industry (2015).

[4] Id.

Toxicological Methods (SACATM) document points out as follows:

> Specifically, legacy test methods and classification systems developed using animal models cannot always evaluate the nuances of human pathophysiology and genetic variability important for modern safety and risk assessment. Ironically, however, the institutionalized use of animal-based methods is now preventing more human-predictive approaches from being developed and adopted by Federal agencies and industry. Left unaddressed, this growing disparity between new scientific advancement and regulatory policy could soon impede our ability to capitalize on the remarkable knowledge and tools arising from projects such as Toxicant, Tox21, Human Tissue Chips, and the Precision Medicine Initiative.

121. In a study spanning 1992-2002, forty-three percent of drugs that passed preclinical animal and other testing later failed during Phase I clinical trials for safety reasons; twenty-five percent of drugs that passed Phase I testing later failed during Phase II clinical trials for safety reasons; and thirty-five percent of drugs that passed Phase II testing later failed during Phase III clinical trials for safety reasons.

122. Indeed, many drugs that have been given to humans after the drug appeared safe in animal studies resulted in severe adverse reactions and death in people.

123. Investigators did not learn the drugs were dangerous to humans through animal testing; they learned the drugs were dangerous to humans through epidemiology, clinical observations, and autopsies.

124. An article recently published in the New England Journal of Medicine states that, because of unexpected toxicities, it takes time and human lives to distinguish toxic effects from manageable effects in clinical trials of new therapies. The article quoted the Children's Hospital of Pennsylvania oncologist and principal investigator of the CART-19 clinical trial in children as saying, "There was no way to predict a great deal of what we learned. The toxicity issues can

only be learned from human beings."5

125. Moreover, legal protection of human subjects has not kept pace with changes in societal ethics.

126. Current FDA regulations governing drug trials require the disclosure of "a description of any reasonably foreseeable risks and discomforts to the subject."

127. Because the regulation does not further specify the content of such disclosure, drug sponsors are able to forego disclosing the fact that preclinical animal testing may not predict the degree of risk to which the trial participants will be subjected.

128. When informed consent regulations were enacted decades ago, society did not have the data it now has as the result of numerous compounds having since been tested through the drug development paradigm.

129. As set forth above, the statistics demonstrate that the preclinical drug development process does not adequately predict either human safety or efficacy.

130. Ethical consideration of this data requires that the informed consent regulations for drug development be updated to reflect the evolution of scientific knowledge that has occurred since the current regulations were adopted.

131. Further, due to the so-called therapeutic misconception, many participants in clinical trials of drugs not only fail to understand the risks involved in the trial, but actually believe that they will potentially receive a personal benefit from the research.

132. In 2001, the National Bioethics Advisory Commission defined the therapeutic misconception as "the belief that the purpose of a clinical trial is to benefit the individual patient

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[5] New England Journal of Medicine, Tragedy, Perseverance, and Chance – The Story of CAR-T Therapy, Lisa Rosenbaum, M.D., September 13, 2017, DOI: 10.1056/NEJMp1711886.

rather than to gather data for the purpose of contributing to scientific knowledge."

133. Indeed, participants have a limited understanding about clinical trials and the core features of clinical research, including the informed consent process and how risks are managed.

134. A study that explored the understanding and expectations of trial participants concerning monitoring and communication of serious adverse events during clinical trials found participants want to have more information disclosed.

135. A 2013 analysis of multiple qualitative studies in the United Kingdom found that participant cooperation with medical research is contingent on participants' belief that investigators will not expose them to harm or exploitation; moreover, participants relied on regulation to enforce this.

136. To meet required ethical standards for disclosure to human subjects participating in clinical trials and offer true informed consent, FDA regulations that govern information given to clinical trial participants must be updated; indeed, history has shown that voluntary guidelines and non-binding principles do not work, and a legal mandate is necessary.

137. The Petitioners provided a detailed, heavily footnoted argument that "FDA Disclosure Standards Should be Analogous to Other Federal Statutory and Other Common Law Disclosure Standards."

138. Physician informed consent requirements under tort law and otherwise mandate that physicians must warn a patient of all potential risks associated with a drug, including all risks that would potentially affect a reasonable patient's decision, regardless of the probability of risk. It was the position of the Petition that current FDA regulations regarding informed consent fall well below what is required for physicians.

139. The disclosure requirements applicable to drug trial subjects under the current

FDA regulation also fall below the disclosure standards mandated by the Federal Trade Commission Act promulgated by the Federal Trade Commission ("FTC"), a sister agency.

140. Under current FDA disclosure requirements, drug sponsors routinely omit information that the average or reasonable consumer would consider material in making an informed decision as to whether to risk his or her health by exposing his or her body to a potentially toxic substance.

141. Specifically, drug trial subjects are misled in clinical trials by the failure of drug sponsors to disclose that animal data is frequently not predictive of human response.

142. Such an omission is likely to mislead a volunteer subject to his or her detriment, as it may result in him or her being unknowingly subjected to physical harm.

143. In an advertisement designed to market a drug to this same individual, an omission of this nature could be construed as false advertising and unfair business practice under FTC rules.

144. For these reasons, regulations that govern clinical drug trials should mandate that investigators make disclosures to drug trial participants that are analogous to the disclosures required by FTC and that patients would receive from their physician if the drug being tested was being prescribed.

145. Generally accepted scientific guidelines applying to all warnings for human subjects participating in research require that the proposed warnings be effective, capture attention, and convey safety attention.

146. The warnings should provide the information that prospective research subjects, such as the Petitioners, need to make judgments regarding the level of risk that they are willing to accept.

147. The Petitioners provided a detailed, heavily footnoted argument that the benefits to the public of the proposed regulation amendment far outweigh any potential challenges.

148. Among other things, they noted that no data exists to support the notion that providing more detailed warnings to potential subjects would decrease participation in human subjects research, and even if this somehow occurred, that may prompt FDA to move more quickly to validate and qualify safe and effective human-derived drug testing methods, and spur on the scientific community's efforts to develop and use more predictive pre-clinical methods.

149. The Petitioners concluded by arguing as follows:

> Trial subjects must receive all information that a reasonable human subject participating in a clinical drug trial would find material. Accordingly, the regulations must be updated to ensure that every prospective trial participant receives the information necessary to evaluate the real risks posed and to provide true informed consent. It is in the best interests of investigators, drug manufacturers, and especially human trial subjects that 21 C.F.R. 50.25 be modified as requested in this petition.

150. On June 19, 2014, DHHS and FDA sent correspondence acknowledging the receipt of the Petition and assigned it docket number FDA-2014-P-0814, styled "Citizen Petition Asking the U.S. Food and Drug Administration to Increase Protection of Human Subjects in Clinical Drug Trials."

151. On or around July 15, 2014, FDA published a Notice in the Federal Register seeking comments on draft guidance entitled "Draft Informed Consent Information Sheet: Guidance for Industrial Review Boards, Clinical Investigators, Availability" ("Draft Guidance").

152. On September 29, 2014, CRS submitted an amendment to the FDA, which included CRS's comments on the Draft Guidance.

153. A true and correct copy of this amendment is attached to this Complaint as Exhibit "B."

154. The amendment stated in part: "CRS supports FDA's efforts to enhance protection for human research subjects. CRS submits this amendment for efficiency purposes because the documents are relevant to one another. This amendment is not submitted to change the content of docket number FDA-2014-P-0814."

155. On December 15, 2014, DHHS and FDA sent what purported to be an "interim response."

156. Therein, DHHS/FDA advised that FDA felt the Petition raised "complex issues requiring extensive review and analysis by Agency officials," and stated that it would "respond … as soon as we have reached a decision on your request."

157. The year 2015 came and went without any further response from FDA.

158. On March 28, 2016, CRS submitted a supplement to the Petition ("Supplement"), along with the exhibits thereto.

159. A true and correct copy of the Supplement to the Petition is attached to this Complaint as Exhibit "C."

160. CRS began by noting that, in the past few months, numerous clinical trials in the United States and abroad were shut down because of severe adverse reactions, including death and permanent disability, in both healthy and patient volunteers.

161. CRS then cited the clinical trial of the drug BIA 10-2474 in France, wherein a previously healthy individual died, and five individuals were hospitalized and faced brain damage, due to severe adverse reactions to the investigational drug.

162. On March 7, 2016, it was reported that experts conducting an investigation had determined that BIA 10-2474 had caused an "astonishing and unprecedented" reaction in the brain that was "unlike anything ever seen before."

163. Before the first tests in humans, BIA 10-2474 had undergone preclinical animal tests in four different species (mice, rats, dogs, and monkeys), using doses 400 times (and in some tests 650 times) stronger than those that would be given to the human subjects.

164. The animal tests did not predict the adverse events in humans, and recent scientific studies by van Esbroeck, et al. show that the drug had an off-target species-specific effect that could not be predicted with traditional animal tests.

165. CRS also cited the TeGenero TGN1412 trial in the United Kingdom, a Phase I trial during which six healthy British men suffered permanent organ damage, and one of them the loss of fingers and toes, from unanticipated severe immune reactions during the testing of an arthritis and cancer drug candidate called TGN1412.

166. Calculation of the starting dose for the Phase I trial was primarily based upon a toxicity study in cynomolgus macaque monkeys, as well as the procedure described in a draft FDA guideline.

167. The Expert Scientific Group (ESG) charged with reviewing the TeGenero tragedy reported: "Species-specificity of an agent does not imply that there is always an increased risk in first-in-man trials, but it makes preclinical evaluation of the risk in animal experiments much more difficult, and sometime perhaps impossible. Therefore, a highly cautious approach is needed."

168. CRS cited additional studies within the United States underscoring concerns about the safety of early-stage human testing, and the need for the proposed amendment.

169. CRS further pointed out that, under § 801 of the Food and Drug Administration Amendments Act, Phase I trials do not have to be registered, and the results of same do not have to be published on the ClinicalTrials.gov web site. This prevents both the public and researchers

from knowing just how often serious adverse events occur in these trials.

170. The Supplement concluded as follows:

> Informed consent is an ethical and legal doctrine that has evolved to protect persons participating in clinical research trials. In light of evolving ethical standards, our increased scientific knowledge, and recent undeniable failures in adequately warning and protecting human clinical trial participants, it is clear that the current informed consent regulations are deficient in the context of drug development, as they do not mandate provision of complete information regarding the risks that human subjects accept when participating in a clinical trial.
>
> Relying on animal models in preclinical development may result in unexpected outcomes since preclinical animal data are often not predictive of human responses. Participation in clinical trials creates a foreseeable risk of harm to humans because subjects are knowingly given investigational products with an incomplete, and possibly incorrect, safety profile derived from animal studies.
>
> Trial subjects must receive all information that a reasonable human subject participating in a clinical drug trial would find material. Accordingly, the regulations must be updated to ensure that every prospective trial participant receives the information necessary to evaluate the real risks posed and to provide true informed consent. It is in the best interests of investigators, drug manufacturers, and especially human trial subjects that 21 C.F.R. 50.25 be modified as requested in this petition.

171. On April 12, 2017, three years after the submittal of the detailed Petition, FDA provided a brief five-page response denying the Petition ("Response").

172. A true and correct copy of the Response is attached to this Complaint as Exhibit "D."

173. FDA's December 15, 2014, interim response claimed that the Petition involved "complex issues requiring extensive review and analysis by Agency officials"; FDA's final Response, dated April 12, 2007, demonstrated that FDA had undertaken little if any review or analysis.

174. FDA began by stating that its informed consent requirements are set forth in 21

C.F.R. Part 50, and that those regulations apply to "all clinical investigations regulated by the [FDA] under sections 505(i) and 520(g) of the Federal Food, Drug, and Cosmetic Act [FD&C Act], as well as clinical investigations that support applications for research or marketing permits for products regulated by the [FDA], including foods, including dietary supplements, [sic] that bear a nutrient content claim or health claim, infant formulas, food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products … ."

175. FDA proceeded to state that, if a clinical investigation involving an FDA-regulated product is conducted or supported by DHHS, then the study is also subject to the Common Rule.

176. FDA then noted that it had issued an "Informed Consent Draft Guidance" on July 15, 2014.

177. FDA then quoted the three new subsections to 21 C.F.R. § 50.25(a) requested within the Petition.

178. FDA then stated, "because the proposed warnings raise broader concerns that make them inappropriate for inclusion in FDA's existing informed consent regulations at 21 CFR part 50, we are denying your petition."

179. FDA then attempted to justify its reasoning.

180. First, FDA stated that the new "warning" statements proposed in the Petition are specific to drug trials, whereas the informed consent regulations in § 50.25(a) apply to clinical investigations involving all types of FDA-regulated products, not just drugs.

181. This rationale for denying the Petition is arbitrary and capricious, an abuse of discretion, and the height of bad faith, as the proposed new regulations would by their own terms only provide "a set of standard warnings in the informed consent document for every phase of

clinical drug trials." (Emphasis added.)

182. Second, FDA stated that the proposed "warnings" would preclude needed flexibility in informed consent discussions.

183. Specifically, according to FDA, "[d]epending on the study and the subject, providing information about the results of any preclinical animal testing that was performed, and information about limitations on the reliability of data from such testing, may or may not be necessary or appropriate."

184. This rationale for denying the Petition is arbitrary and capricious, an abuse of discretion, and an irrational, bad-faith departure from its prior position.

185. For example, a 2006 FDA news release stated as follows (emphasis added): "Currently, nine out of ten experimental drugs fail in clinical studies because we cannot accurately predict how they will behave in people based on laboratory and animal studies," and in 2004, FDA reported that ninety-two out of 100 drugs that successfully pass preclinical animal testing subsequently fail during clinical trials when the drug is tested in humans.

186. In a study spanning 1992-2002, forty-three percent of drugs that passed preclinical animal and other testing later failed during Phase I clinical trials for safety reasons; twenty-five percent of drugs that passed Phase I testing later failed during Phase II clinical trials for safety reasons; and thirty-five percent of drugs that passed Phase II testing later failed during Phase III clinical trials for safety reasons.

187. Indeed, FDA is well aware that many drugs that have been given to humans after the drug appeared safe in animal studies resulted in severe adverse reactions and death in people. In fact, there have been at least 154 treatment-related deaths in all phases of human clinical trials in the U.S. since 2012, plus many instances where "multiple deaths" and "unknown" number of

deaths were reported, so the number is likely much higher. Unambiguous and complete reporting of the number of deaths in trial registries and publications does not currently exist. Incomplete public information on clinical trial deaths can be found in media reports and Securities and Exchange Commission (SEC) filings, mainly reported in the context of stock implications for the drug sponsor.

188. Clinical Trial Treatment-Related Deaths

2016-2017 – 143+
2014-2015 – 10+
2012-2013 – 1+

Date Reported	Drug/Company	Deaths	Phase/Cause
2017	Juno Therapeutics, Inc. Transcend Lymphoma Trial JCAR017	1	Diffuse alveolar damage
2017	Stemline Therapeutics	4	Capillary Leak Syndrome Phase II
2017	Kite Pharma ZUMA-1 CAR-T	1	Cerebral Edema brought on by Cytokine Release Syndrome
2017	Ionis Pharmaceuticals – inotersen	1	Intracranial hemorrhage Phase III
2017	Merck Keytruda Keynote-183	29	Phase III Myocarditis, Stevens-Johnson syndrome, myocardial infarction, pericardial hemorrhage, cardiac failure, respiratory tract infection, neutropenic sepsis, sepsis, multiple organ dysfunction, respiratory failure, and unknown.
2017	Merck Keytruda Keynote-185	19	Phase III intestinal ischemia, cardio-respiratory arrest, suicide, pulmonary embolism, cardiac arrest, pneumonia, sudden death, myocarditis, large intestine perforation, and cardiac failure.
2017	Seattle Genetics Vadastuximab talirine	Undisclosed	Undisclosed
2017	Bristol-Myer Squibb nivolumab (Opdivo) Approved by FDA 2/17	4	Unknown

Date Reported	Drug/Company	Deaths	Phase/Cause
2017	Takeda – bigatinib ALUNBRIG Approved by FDA 4/17	8	Phase II Pneumonia (2), Sudden death (1) Dyspnea (1), Respiratory Failure (1) Pulmonary embolism(1), Bacterial meningitis (1), Urosepsis (1)
2017	Johnson & Johnson Sirukumab FDA voted against approval 8/2/17	34	All phases Cardiovascular events (13), Serious infections (8), Malignancies (6) Other (9)
2017	Cellectis UCART123 FDA clinical hold 9/4/17	1	Phase I Cytokine release syndrome and capillary leak syndrome
2017	Alnylam Pharmaceuticals Fitusiran for hemophilia A and B	1	Mid-stage Blood clot cerebral venous sinus thrombosis (CVST)
2016	BIA 10-2474 BIAL	1	Phase I unprecedented reaction in the brain
2016	Juno Therapeutics Inc. JCAR014 for Adult ALL	2	Cerebral Edema and Cytokine Release Syndrome or neurotoxicty
2016	Juno Therapeutics Inc. JCAR014 for Lymphoma	1	Cytokine Release Syndrome or neurotoxicity
2016	Juno Therapeutics Inc. JCAR014 for CLL	1	Cytokine Release Syndrome, cerebral edema
2016	CTI Biopharma Pacritinib	Unknown	Intracranial hemorrhage, cardiac failure, cardiac arrest
2016	Gilead Sciences Zydelig	Multiple	Infections
2016	Juno Therapeutics, Inc. Rocket Trial JCAR015	3	Phase II Cerebral Edema brought on my Cytokine Release Syndrome
2016	Alnylam Pharmaceuticals givosiran	3	"early stage" hemorrhagic pancreatitis and pulmonary embolism
2016	Ziopharm Oncology Ad-RTS-hIL-12	3	Phase I Intracranial hemorrhage (1) Other two deaths unknown
2016	Alnylam Pharmaceuticals revusiran	17	Phase III Undisclosed cause of death
2016	Juno Therapeutics, Inc.	2	Phase II Cerebral Edema brought on by

Date Reported	Drug/Company	Deaths	Phase/Cause
	Rocket Trial JCAR015		Cytokine Release Syndrome
2016	Seattle Genetics	4	Hepatoxicity Phase II
2016	Kite Pharma ZUMA-1 CAR-T	3	hemophagocytic lymphohistiocytosis, cardiac arrest in the setting of Cytokine Release Syndrome and pulmonary embolism)
2015	Zafgen Inc. – beloranib	2	Pulmonary emboli
2015	Juno Therapeutics Inc. JCAR014	1	Encephalopathy Cytokine Release Syndrome
2014	Juno Therapeutics, Inc. Rocket Trial JCAR015	3	Phase I Cytokine Release Syndrome
2014	Juno Therapeutics, Inc. JCAR014 for Adult ALL	1	Cytokine Release Syndrome
2014	Novartis University of Pennsylvania CAR-T Study for Leukemia	3	Cytokine Release Syndrome and Sepsis
2012	Bristol-Myers Squibb BMS-986094	1	Phase II Cardiac

189. FDA is also fully aware that investigators did not learn the drugs were dangerous to humans through animal testing; they learned the drugs were dangerous to humans through epidemiology, clinical observations, and autopsies.

190. FDA failed to acknowledge its previous agency announcements, policies, and practices acknowledging significant, across-the-board issues with the predictive nature of animal testing, much less explain why FDA was deviating from that precedent.

191. Third, and finally, FDA stated that it is developing "guidance" that addresses the issues raised in the Petition.

192. This rationale for denying the Petition is arbitrary and capricious, and an abuse of discretion, and provides no recognized grounds for agency inaction.

193. CRS submitted comments to FDA's proposed Draft Guidance on September 11, 2014, and also submitted the comments to FDA to be filed in the citizen's petition docket as an amendment. CRS noted in the amendment, "This amendment is not submitted to change the content of docket number FDA-P-0814."

194. The Petition specifically requests regulation changes, because guidance documents do not carry the weight that regulations carry.

195. Indeed, protection of clinical trial participants requires more than guidance.

196. Additionally, FDA has a history of promising guidance instead of regulation change when denying a citizen's petition, and not following through.

197. Indeed, the June 2016 issue of the Regulatory Affairs Professional Society newsletter, Driving Regulatory *Excellence*, noted as follows (emphasis added):

> The US federal government is notoriously slow at promulgating new rules and bringing them into enforcement. But the US Food and Drug Administration (FDA) is taking that slowness to a whole new level for a host of potentially controversial final and proposed rules, some of which have lingered for decades. ... One of the prime examples of such a lengthy delay is for a final rule dealing with new postmarket safety reporting requirements for human drugs and biologics. First proposed in 2003, HHS now says FDA will need until March 2017 ... to take final action on the rule, which would further harmonize certain definitions and reporting formats with those used by the International Conference on Harmonisation. The complete list of rules and their prospective dates, many of which get pushed back without any transparency or explanation, comes as Republican senators have taken issue with the way FDA is using draft and final guidance to regulate, rather than via rule makings.

198. Moreover, a June 2016 report from the U.S. Government Accountability Office concluded as follows: "The Food and Drug Administration (FDA) lacks measurable goals to assess its progress in advancing regulatory science—the science supporting its effort to assess the products it regulates."

199. In light of the large number of recent deaths and serious adverse events suffered by trial participants, these delay tactics by FDA are particularly egregious and indefensible.

200. In a 2010 denial of a citizen's petition6 filed by the "MAP Coalition" in 2007, FDA committed to issuing guidance regarding the use of non-animal test methods. FDA stated "FDA intends to issue a draft guidance to industry and FDA staff regarding the use of NATMs."7 FDA asserted that guidance would negate the need for regulations.

201. Documents provided by FDA in a response to a Freedom of Information Act request show that little or no effort was made to draft the promised guidance.

202. Despite the commitment and meeting with the petitioners therein on several occasions for discussions on development of the guidance, four years later FDA informed the petitioners therein that guidance would not be issued.

203. FDA's response to the Petition has harmed the individual Plaintiffs.

204. The Plaintiffs herein are interested in, adversely affected by, and substantially aggrieved by the final agency action challenged herein, and have the necessary standing to challenge same. Accord 21 C.F.R. § 10.25(a) ("An interested person may petition the Commissioner to issue, amend, or revoke a regulation or order, or to take or refrain from taking any other form of administrative action."); id. § 10.45(d)(ii) ("An interested person is affected by, and thus has standing to obtain judicial review of final agency action.").

205. Indeed, each of them has been harmed by FDA's continued failures to expressly require the disclosures at issue, which are amply supported by medical and scientific evidence.

206. The absence of such disclosures within informed consent documentation caused or

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[6] Docket No. FDA-2007-P-0109

[7] Letter from David H. Dorsey, Acting Deputy Commissioner for Policy, Planning and Budget, Food and Drugs to Katherine Meyer, Meyer Glitzenstein & Crystal 3-4 (May 20, 2010).

contributed to the tragic death of Max Vokhgelt, and exposed and continues to cause the other individual Plaintiffs to be exposed to great personal risk.

207. Had Max and his family been provided with adequate disclosure, they would have had the informed option to decline participation in the trial, thus avoiding Max's premature death, and Michael Vokhgelt suffers from anxiety and fear with regard to his other children's potential need to participate in human subjects research without complete disclosure of the risks.

208. Mr. Tessmer and Mr. Garcia-Smith are unable to participate in trials because they now know that they are not given complete disclosure of the risks; this takes away Mr. Garcia-Smith's capability of participating for altruistic reasons, namely supporting his community, and harms Mr. Tessmer financially.

209. Further, CRS has organizational standing because the interests at stake are germane to CRS's purposes, and FDA's response will require further extensive advocacy work on the part of CRS, placing a significant drain on its limited resources, causing a diversion of its resources, and the frustration of its mission.

210. Indeed, in the absence of the amended regulation, it would cost CRS a substantial sum of money to educate and protect the welfare of potential clinical trial participants nationwide about the issues with animal testing discussed in detail herein, when the actual legal responsibility for doing so lies with FDA.

211. Each of the Plaintiffs is aggrieved on a continuing and ongoing basis by the harm caused by FDA's actions as described herein, and the relief sought in this Complaint will redress the injury suffered by each of the Plaintiffs that is caused by FDA's actions as described herein.

COUNT ONE – CHALLENGE UNDER THE ADMINISTRATIVE PROCEDURE ACT

212. The Plaintiffs incorporate the foregoing paragraphs as if set forth fully herein.

213. This is a challenge under the Administrative Procedure Act, and such other

authorities as are applicable, to the denial by FDA of the citizen petition asking FDA to "add … Sections (9) – (11) to 21 C.F.R. § 50.25(a), providing a set of standard warnings in the informed consent document for every phase of clinical drug trials."

214. The Plaintiffs herein seek injunctive relief requiring the Defendant/FDA to approve the new regulations, or such equitable relief as the Court may deem to be appropriate, and a declaratory judgment that FDA's denial violates the APA, and such other authorities as are applicable.

215. FDA's denial of the Petition is arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law, in violation of 5 U.S.C. § 706(2)(a), and such other authorities as are applicable, in general and for the reasons stated with specificity above.

216. FDA's denial of the Petition exceeds its statutory authority in violation of 5 U.S.C. § 706(2)(c) in that is decision was improperly and impermissibly motivated by factors other than medicine and science.

217. FDA's denial of the Petition is not supported by medical or scientific evidence.

218. FDA's denial of the Petition is not supported by the agency record.

219. FDA's denial of the Petition was scientifically unjustified, and contrary to agency precedent.

220. FDA's denial of the Petition was made in bad faith, and it conducted itself in bad faith in connection with the consideration of the Petition.

221. FDA's denial of the Petition otherwise violates the Administrative Procedure Act.

222. Recently, in Flyers Rights Education Fund, Inc. v. Federal Aviation Administration, – F.3d – (D.C. Cir. 2017), the D.C. Circuit reiterated the principle that "the Administrative Procedure Act requires reasoned decision-making grounded in actual evidence."

223. Flyers Rights involved a citizen's petition to the Federal Aviation Administration ("FAA") pursuant to 49 U.S.C. § 106(f)(3)(A) and 14 C.F.R. § 11.61(a).

224. In their petition, a non-profit group advocating for the rights of individuals who fly commercially, as well as its president (collectively, "Flyers Rights"), petitioned FAA "to promulgate rules governing the minimum requirements for seat sizes and spacing on commercial passenger airlines."

225. The petition noted that the "seat pitch" of an economy-class seat has decreased from an average of thirty-five inches to thirty-one inches, and the seat width of an economy-class seat has decreased from approximately eighteen and a half inches to seventeen inches, while all the while "the average American flyer has grown steadily larger in both height and girth."

226. Flyers Rights expressed concern "that the decrease in seat size, coupled with the increase in passenger size, imperiled passengers' health and safety by slowing emergency egress and by causing deep vein thrombosis," a potentially fatal condition.

227. FAA denied the petition without challenging Flyers Rights' characterization of seat dimension decreases or passenger size increases, much less citing any studies or tests to corroborate its conclusions.

228. Subsequently, at Flyers' Rights request, FAA provided citations to studies, but those studies "did not address the impact of smaller seat dimensions of increased passenger size on the ability of passengers to expeditiously leave their seats and reach the emergency exits."

229. On appeal, the D.C. Circuit noted that FAA "has a broad mandate to protect and promote passenger safety," and "[a]ccordingly, when the [FAA] responds to a petition for rulemaking that exposes a plausible life-and-death safety concern, the [FAA] must reasonably address that risk in its response." (Emphasis added.)

230. The D.C. Circuit readily held that FAA had failed to do so, and remanded the matter back to FAA.

231. In this case, for all of the reasons set forth in detail above, the Petition "exposes a plausible life-and-death safety concern," and FDA's curt denial of the Petition in a five-page letter is unsupported by reasoned decision making grounded in actual evidence.

WHEREFORE, the Plaintiffs respectfully demand the following relief:

1. A judgment in their favor, and against the Defendant;

2. An injunction ordering FDA to approve the Petition, and "add … Sections (9) – (11) to 21 C.F.R. § 50.25(a), providing a set of standard warnings in the informed consent document for every phase of clinical drug trials," in general and as described more specifically herein;

3. A declaratory judgment that FDA's denial of the Petition violates the APA, and such other authorities as are applicable;

4. Attorney's fees, litigation expenses, court costs; and

5. Such other relief as is just and proper in the circumstances presented.

Dated: October 23, 2017

Respectfully submitted,

SHERMAN, SILVERSTEIN, KOHL, ROSE & PODOLSKY, P.A.

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