U.S. FOOD & DRUG ADMINISTRATION

January 15, 2025

Nina Zeldes, Ph.D
Health Researcher
Public Citizen's Health Research Group

Robert Steinbrook, M.D.
Director
Public Citizen's Health Research Group

Dear Drs. Zeldes and Steinbrook,

Thank you for your letter, dated December 13, 2024, to Dr. Califf, Commissioner, Food and Drug Administration, regarding the conduct of the Alzheimer's disease trials for lecanemab and donanemab and the actions of the Institutional Review Boards with oversight over these studies and the informed consent documents. Your letter was received by Dr. Califf and shared with the Center for Drug Evaluation and Research for response.

The Food and Drug Administration (FDA) takes the safety and wellbeing of clinical trial participants very seriously. FDA protects the rights, safety, and welfare of human subjects participating in clinical trials by assessing compliance with clinical research protocols and the standards for good clinical practice in clinical research.

It is important to consider the context of what was known about amyloid-related imaging abnormalities (ARIA) at the time that the informed consent forms were initially drafted for the clinical trials for lecanemab and donanemab over 5 years ago. The understanding of the connection between ApoE4 homozygotes and serious adverse outcomes relating to ARIA has evolved over the last several years.

We recognize that it can be challenging to determine how risks should be framed in an informed consent document, particularly in a situation when clinical trials spanned several years while the understanding of the science evolved. The role of the institutional review board (IRB) is to have a committee of individuals, with differing expertise and perspectives, including scientists and lay persons, consider the proposed consent form language to determine if it properly informs potential trial subjects of the risks of their participation. FDA is responsible for assuring that IRBs are properly constituted and follow the appropriate regulations governing IRBs (see 21 CFR Part 56); these rules provide detailed information about the form, processes, and functions of an IRB so as to assure a thorough review of trial risks and patient consent forms.

Concerning investigations, as a general policy, the FDA does not disclose its thinking regarding, nor does it confirm or deny, potential or ongoing investigations or inspections. FDA takes appropriate action if we find potential violations of the laws in place to protect human subjects participating in clinical trials.

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Thank you, again, for sharing your concerns.

Sincerely,

Patrizia A. Cavazzoni -S

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Patrizia Cavazzoni, M.D.
Director
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