PhysiciansCommittee
for Responsible Medicine
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March 28, 2023

Donna L. Mendrick, Ph.D., Designated Federal Officer
National Center for Toxicological Research
10903 New Hampshire Avenue
Building 32, Room 2208
Silver Spring, MD 20993-0002

Re. Docket ID: FDA-2023-N-0217

Dear Dr. Mendrick:

The Physicians Committee for Responsible Medicine (PCRM) thanks the Food and Drug Administration (FDA) for the opportunity to comment on its Science Advisory Board (SAB) to the National Center for Toxicological Research (NCTR) Advisory Committee meeting. PCRM is a nonprofit organization comprised of nearly one million members and supporters worldwide advocating for efficient, effective, and ethical medical practice, nutrition, and research.

To support its Predictive Toxicology Roadmap (PTR) and advance alternative methods, in its fiscal year 2024 justification of appropriations, FDA highlights the need for comparative assessments between traditional animal-based testing and emerging technologies to ensure the reliability of new, non-animal methods for product development and regulatory decision-making. Although PCRM supports the acceptance of such methods that both enhance predictive capabilities and reduce animal use, we are concerned that FDA may use these funds to conduct new animal testing.

Due to the limitations of animal-based testing, which include high variability in test results and species differences in physiology and metabolism, non-animal methods should be compared to effects in humans whenever possible. For example, defined approaches for skin sensitization, which combine non-animal methods with computational models, were compared to human patch tests and existing data from Local Lymph Node Assays (LLNAs) in mice. These comparisons revealed that the defined approaches were more predictive of human effects than were the LLNAs. When adequate information on effects in humans is unavailable, it is preferable to compare non-animal methods to existing data from traditional animal-based testing to be consistent with the goal of reducing animal use. PCRM urges FDA to reconsider this approach to ensuring the reliability of non-animal methods and to adopt a strategy that avoids conducting new tests using additional animals.

In addition, PCRM commends NCTR for emphasizing the development of emerging technologies in its 2021 annual report; however, we are concerned by ongoing projects in the Division of Biochemical Toxicology that included studies of nicotine and cannabidiol in rats. Due to the limited information available on these projects, we were unable to assess the Division's rationale for conducting new studies on substances for which toxicity in animals has already been evaluated extensively. To prevent duplicative testing, PCRM recommends that NCTR publicize its research proposals prior to initiating them. For example, the National Toxicology Program typically provides materials and solicits public

comment on new research programs for chemical nominations during its Board of Scientific Counselors meetings; NCTR could include similar discussions at its SAB. Finally, to measure progress toward achieving FDA's PTR goals, PCRM requests that NCTR track its animal use and discuss it in its annual reports and at its SAB. By adopting such transparent practices, FDA and NCTR can reduce animal use while better protecting public health.

Thank you for your attention to these comments.

Sincerely,

Joseph Manuppello
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