Dear Dr. Collins:

Public Responsibility in Medicine and Research (PRIM&R) appreciates the opportunity to comment on the Request for Information: Invitation to Comment on Inclusion in Clinical Research Across the Lifespan, published on April 26, 2017, by the National Institutes of Health (NIH).

Since its founding in 1974, PRIM&R has been dedicated to advancing the highest ethical standards in the conduct of biomedical, behavioral, and social science research. We accomplish this mission through education, membership services, professional certification, public policy initiatives, and community building.

PRIM&R applauds NIH for seeking public input on the appropriate inclusion of pediatric and older populations in research studies involving human subjects. PRIM&R also supports NIH’s desire—clear in the wording of the RFI and in the proceedings of the meeting held on June 1-2 on this topic—to facilitate greater inclusion of previously under-represented groups in research. Despite repeated efforts directed at reducing barriers to broad inclusion in research, many groups remain understudied, including the elderly, children, individuals who are mentally ill or cognitively impaired, women of child-bearing age and potential, and pregnant women. The broad concept of justice demands the responsible inclusion of such populations in research so that they may benefit from scientific advancement.

While PRIM&R fully supports efforts to promote research involving pediatric and elderly populations, we want to take this opportunity to emphasize that there are ethically important considerations relevant to their inclusion in research. Specifically, as efforts in this regard move forward, we urge NIH to bear in mind the following two points.
First, chronological age itself does not indicate susceptibility to risk or vulnerability to undue influence. At any age, an individual’s capacity to engage in the informed consent process and assess the risk and benefit of research participation will vary depending on a range of cognitive abilities and situational factors. Research with individuals at various points in the lifespan may also introduce risks that are uniquely associated with that age group—consider, for example, neonates, adolescents, and the “old-old.” Therefore, the ethical inclusion of subjects across the lifespan requires the recognition of common vulnerabilities and risks within each stage of life while identifying the impact of specific conditions and circumstances on each individual.

Second, research with individuals from groups understudied or excluded because of a likelihood of impairment in consent capacity requires appropriate additional safeguards in review, in consent procedures, and research design in general. While current regulations—specifically 45 CFR 46 subpart D—outline such protections and safeguards for children, no analogous regulations or formal guidance have been developed for adults with cognitive impairment, despite recommendations from the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (in 1978) and from the National Bioethics Advisory Commission (in 1998).

Inclusion of these populations in research will thus require appropriate oversight. Necessary safeguards might include initial and ongoing identification of impairment in decision-making capacity, efforts to secure a legally authorized representative for those in whom cognitive decline is anticipated, and the engagement of family and other caregivers in the ongoing research process. Of course, the actual safeguards that should be developed and implemented will necessarily need to be tailored to study risk and the particular population.

Fortunately, the ethical grounds as well as the practical barriers and opportunities for including a wide range of under-represented groups in research has been described and deliberated for quite some time. There is a robust body of scholarship and policy recommendations on these issues to be found in the work of a number of national bioethics advisory groups. Rather than address these issues de novo, we encourage NIH to revisit and review these existing reports. In particular, we draw your attention to three reports: the National Bioethics Advisory Commission’s report, Research Involving Persons with Mental Disorders That May Affect Decisionmaking Capacity—which specifically addresses the need to avoid treating groups with mental disorders as monolithic; the Presidential Commission for the Study of Bioethical Issues’ report on Gray Matters: Topics at the Intersection of Neuroscience, Ethics, and Society (specifically recommendations six through nine); and the Secretary’s Advisory Committee on Human Research Protections, Recommendations Regarding Research Involving Individuals with Impaired Decision-making. As noted earlier, although the recommendations from these federal bodies have not been adopted as official
federal policy or regulation, they resonate with, and promise to enhance the value of, NIH's stated objective to make progress on this matter.

We hope that our input will prove useful to NIH as it continues its work on inclusion in research across the lifespan. If you have any questions about our comments, or require any further information, please feel free to contact me at (617) 303.1872 or ehurley@primr.org, or the chair of PRIM&R's Public Policy Committee, Dr. David H. Strauss at strauss@nyspi.columbia.edu.

Sincerely,

Elisa A. Hurley, PhD
Executive Director

cc: Board of Directors