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Request for Information: Soliciting Input on Opportunities, Gaps, and Challenges in Global Health Research in Neurological Diseases and Stroke

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The most impactful research opportunities for addressing global neurological health needs

Addressing global neurological health needs must take a human-first approach. This should include reforms aimed both at improving access to neurological health care and ensuring that neurological research is conducted using human-relevant systems, not poorly predictive animal models. According to the World Health Organization, "Over 80% of neurological deaths and health loss occur in low- and middle-income countries, and access to treatment varies widely: high-income countries have up to 70 times more neurological professionals per 100 000 people than low- and middle-income countries." It is crucial that NINDS support the expansion of properly staffed health care systems in LMICs. Correcting this access disparity would go a long way towards reducing neurological deaths. In addition, according to NIH RePORTER, NINDS is currently administrating 1,935 active projects, accounting for \$1,132,077,018 in federal funding, for experiments that use animal models. NINDS must transition funds away from the use of animals as models for human conditions and toward more predictive, human-based methodologies. Experiments on animals overwhelmingly fail to capture the specific etiological and physiological features of human neurological diseases and are inconsistent in the pathological and behavioral phenotypes displayed. Use of these models has been cited as a factor in the failure of so many new drugs in clinical trials (for example, 99.6% failure for Alzheimer's disease and 100% failure for stroke). In contrast, methods based in human biology are increasingly found to be more predictive than experiments on animals. These include methods that use human brain samples or human cells, human -omics data, neuroimaging, biological engineering, and advanced computer modeling. Examples of these technologies and why they should replace the use of animals are available in our Research Modernization Deal (see pages 30-32 (neurodegenerative diseases) and pages 33-35 (stroke)). There are also animal welfare and logistical reasons for NINDS to cease funding of experiments on animals that take place outside of the U.S. A PETA expose of an NIH-funded research center in Colombia revealed horrific animal abuse and research misconduct that resulted in the closing of the center, the rescue of over 200 monkeys and mice, the ineligibility of the center to receive future NIH grants, and a more than \$200,000 fine by the country's environmental agency. OLAW has no oversight over foreign laboratories thus no way to ensure that these facilities are upholding the minimum standards of PHS Policy and the Animal Welfare Act.

Strategies to build and improve sustainable neurological research capacity at LMIC academic/research institutions, including for basic, translational, and clinical research

Research capacity in LMICs can be improved by ensuring that the scientists trained in these institutions receive the most up-to-date education to prepare them for the future of biomedical research. This training is addressed in the next response. To build capacity for human-relevant research and its training, NINDS should assist LMICs in the establishment of national centers or core facilities to provide researchers with access to resources and experts in the use of non-animal methods. These could include biobanks and centers for microphysiological systems, three-dimensional cell culture, three-dimensional tissue printing, animal-free antibodies, or advanced computing including the use of AI to complement human research. NINDS should cease to fund centers or facilities that specialize in the use or creation of animal models.

The most important training needs and/or most promising training approaches in global neurological research, including how best to support a pipeline of trained scientists and health professionals in neuroscience

As the field of animal-free research continues to expand, increased education and hands-on training will accelerate the transition to these methods. It is crucial that human-relevant educational initiatives be adopted and given ample financial support across the whole neurological research sector, including academia, scientific and funding communities, and industry, from future scientists to established professionals. Scientists in LMICs must be provided with opportunities to develop the skills necessary to contribute to the field of human-relevant neurological research so that their communities can compete with international developments. Because many educational programs lack sufficient courses about animal-free methods, supplemental training programs have been developed. For example, in the EU, the European Commission's Joint Research Centre hosts a summer school on non-animal approaches. Similar programs could be replicated in LMICs. Many online resources by experts in the field also exist, including those offered by PETA Science Consortium International e.V. and the Physicians Committee for Responsible Medicine. Thus, information about animal-free research and testing is available and should be a component of all scientific education. Awareness among scientists of animal-free methods may be increased through the creation of national centers of competences for animal-free research, tenure tracks and professorships based on non-animal methods, and animal-free research officer positions to advise professors, staff, and students. Universities and other academic institutions in LMICs could also be encouraged to develop a departmental body to oversee the transition to animal-free research that can work and advise across different departments. Such bodies could help organize Ph.D. and postgraduate programs that use only non-animal methods as well as workshops, seminars, and summer schools on *in vitro* and *in silico* methods. As the field of animal-free testing methods continues to expand, researchers must keep pace with these pivotal developments. Increased education and training initiatives are urgently required to build confidence in reliable and relevant non-animal methods that can best protect human neurological health.