BRAIN Initiative
Neuroethics Working Group Pre-Meeting for Continuing Trial Responsibilities Workshop

Perspectives from Device Manufacturers, Investigators, and Regulators

December 17, 2021

Virtual Meeting

Draft January 3, 2022

This meeting summary was prepared by Rose Li and Associates, Inc., under contract to the National Institute for Neurological Disorders and Stroke (NINDS). The views expressed in this document reflect both individual and collective opinions of the meeting participants and not necessarily those of NINDS. Contributions to this meeting summary by the following individuals are gratefully acknowledged: Christina Tricou, Caroline Sferrazza, Nancy Tuvesson.

Executive Summary

On December 17, 2021, the Neuroethics Working Group (NEWG) of the Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative held a pre-meeting for a 2022 Continuing Trial Responsibilities Workshop. The workshop will focus on research-related trial care responsibilities for participants in clinical trials involving implantable neurological devices and will include perspectives from the National Institutes of Health (NIH), health insurers, device manufacturers, patients, researchers, regulators, and bioethicists. Furthermore, the workshop topics will reflect the collective belief that key stakeholder groups involved in clinical trials hold a shared responsibility to facilitate research-related trial care, yet how that care should be facilitated remains unclear.

During this series of pre-meetings, NINDS will convene relevant stakeholders to gather information that will shape the Continuing Trial Responsibilities Workshop. This pre-meeting featured the perspectives of device manufacturers, investigators, and regulators. Topics highlighted as relevant to this stakeholder group included (1) the maintenance of safety and follow-up care, including necessary explants; (2) the financial challenges of post-trial care; (3) the need to develop broadly accepted standards for research-related trial care; (4) the need to share care responsibilities among stakeholders; and (5) the possibility of using existing commercial hardware in clinical trials when possible to limit the exposure of patients to the investigational landscape. All participants agreed that the aim of research-related trial care is to "do the right thing" by their patients.

Current Landscape of Research-Related Trial Care Facilitation

No official framework currently exists for the care of study participants who choose to keep implanted devices and thus require ongoing care, or for participants who require explantation—leaving investigators to develop post-trial care plans independently. In the former case, care responsibilities are often distributed arbitrarily among investigators, insurers, and medical centers. In the latter case, the impetus for explantation typically determines the payor; if it is medically indicated (e.g., infection or malfunction), the insurer will usually pay. However, investigators often need to cover the cost of elective explants, and hospitals may need to absorb the cost of the procedure without reimbursement if research funds were not set aside for this purpose. The relationship between hospitals and investigators may thus be damaged when the financial responsibility for post-trial care is poorly planned, potentially complicating future care or trials.

A device's investigational or commercial approval status can also influence the financial landscape of post-trial care. Insurers generally pay for continuing medical care if a device is commercially approved following a trial. Similarly, the Centers for Medicare & Medicaid Services (CMS) has established policies that strongly support investigational devices, and private insurance companies generally follow the same policies. Thus, device companies and investigators are typically the payors of last resort for care involving on-label use of investigational devices.

However, the patient may experience gaps in financial coverage if they seek care long after a study ends, and reimbursement for care related to off-label use of an investigational device is difficult to obtain. In addition, use of commercially available devices may be reimbursed if prescribed off-label, but not if the device is being used in an investigational capacity for a new indication in a clinical trial.

When insurers do not reimburse the cost of post-trial care, private device companies often cannot assume the full cost alone. The company's original trial grant funds may be depleted, or the company may no longer exist. Furthermore, private companies frequently rely upon venture investors, who benefit from companies "failing fast;" that is, if investors can terminate relationships with a company early, then they can invest elsewhere. This approach renders the interests of venture investors incompatible with the ongoing investment necessary for post-trial care. One strategy to navigate this challenge is to create a trust, but administration of a post-trial care trust is not straightforward in the clinical trial research community.

Minimum Requirements for Research-Related Trial Care and Areas for Improvement

All parties involved in clinical device trials should err on the side of benefiting the patient. Thus, participants who wish to keep their devices should be encouraged to do so, and no person should force explantation. The only external influence on a participant's choice to explant their device should be the company's ability to provide technical support and maintenance. Routine care after a trial is relatively easy to provide and generally reimbursed by insurance. However, reimbursement for off-label use of investigational devices or device-related care is more elusive. Device manufacturers generally provide replacement devices to former trial participants if necessary, but the hospital may require compensation for the procedure; this gap is one source for potential improvement with stakeholder collaboration.

Currently, device manufacturers can facilitate post-trial care through several means. Following a device's approval, provision of replacement parts or devices is usually simple. However, such provision is extremely difficult after a manufacturing line has been dismantled, as may be done after a clinical trial concludes, a company is sold, or a company ceases to exist entirely. Companies could reduce the impact of this problem by designing devices with backward compatibility. Another strategy, particularly with regard to partial replacements, is to develop compatibility standards across companies; however, the prospect of interchangeable components for implantable neurologic devices remains unachievable in the current environment.

To support study participants who no longer wish to keep an investigational device, funds should be available for elective explants and other post-trial care beyond the clinical trial. Clear financial expectations for each stakeholder would assist device companies in determining the amount of money to designate for this purpose, and, by extension, the financial feasibility of trial and associated post-trial care. Ultimately, the best financial strategy for post-trial care may be a commercially or federally managed trust, escrow, or insurance fund for neurologic or other

implanted devices, which would safeguard funds for elective explants even if the original device manufacturer no longer exists.

Currently, the clinical research community lacks clear and standardized guidelines for post-trial care expectations, without which investigators must develop policies individually for each study they conduct. A new investigator should have guidance for post-trial care, and a trial participant should know what to anticipate from a device manufacturer or researcher for their specific type of device (e.g., permanently implantable or prosthetic devices). Training workshops or other strategies that support investigators to think beyond the immediate grant application and address patient needs after the trial's end would benefit all clinical device trial participants. Further, when patients are informed by published standardized guidelines, they can more effectively advocate for themselves.