Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Neuroethics Working Group (NEWG) Workshop on Continuing Trial Responsibilities

National Institute of Neurological Disorders and Stroke

May 24-25, 2022

Virtual Meeting

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Acronym Definitions

BRAIN	Brain Research Through Advancing Innovative Neurotechnologies
CDMRP	Congressionally Directed Medical Research Program
CED	Coverage with Evidence Development
CMS	Centers for Medicare and Medicaid Services
DBS	Deep Brain Stimulation
FAQ	Frequently Asked Questions
FDA	Food and Drug Administration
FOA	Funding Opportunity Announcement
IDE	Investigational Device Exemption
IRB	Institutional Review Board
LGS	Lennox-Gastaut Syndrome
MEDCAC	Medicare Evidence Development and Coverage Advisory Committee
MRCT	Multi-Regional Clinical Trials
NEWG	Neuroethics Working Group
NIH	National Institutes of Health
NINDS	National Institute for Neurological Disorders and Stroke
PI	Principal Investigator
RNS	brain-responsive neurostimulation
SSDI	Social Security Disability Insurance
VICP	Vaccine Injury Compensation Program

Table of Contents

Executive Summary

The Neuroethics Working Group (NEWG) of the Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative held a Workshop on Continuing Trial Responsibilities on May 24-25, 2022. This workshop convened stakeholders of clinical trials involving implantable neurological devices, including representatives from the National Institutes of Health (NIH), health insurers, device manufacturers, patients, caregivers, researchers, regulators, and bioethicists. Meeting participants were tasked with discussing expectations for post-trial care plans that could inform best practices for the neurotechnology clinical trials research community.

Typically, post-trial care is characterized as the care provided to patients after a trial's end and before the device has received regulatory approval. Patients may also require post-trial assistance if (1) a device does not receive regulatory approval, (2) a device manufacturer discontinues the device or closes entirely, (3) a patient lacks insurance coverage, or (4) standard financial support structures disappear unexpectedly (e.g., the lead investigator moves to a new institution). Overall, the post-trial period is a critical time to provide appropriate care to patients; however, the responsibilities for providing and funding this care are unstandardized and unclear.

What needs may study participants have in relation to their trial participation after a trial ends?

Discussants agreed that, after a trial concludes, patients may have the following needs: (1) continued access to an already implanted device, (2) emergency care due to unexpected adverse events, (3) coordination of care, follow-up care, (4) device maintenance (e.g., access to specialized clinicians, compatible software, compatible hardware or replacement parts, and associated surgeries), (5) elective or medically indicated explantation, (6) device replacement, (7) psychological support, (8) clear explanations of future care and expense, and (9) approaches to share research records with other providers and patients. Providing patients with contingency plans in the event of possible explantation may support their decision-making autonomy. Facilitating connections among patients may benefit overall wellbeing.

To sufficiently prepare patients for post-trial life, research teams should ensure that clinical trial plans account for different levels of support that diverse participants (e.g., of different socioeconomic statuses) may need. Clinical trial teams should consider patients' lifetime care needs during device design (e.g., rechargeable batteries); provide patients with layperson-appropriate informed consent information; and develop follow-on studies that evaluate patient outcomes and safety.

What do different stakeholders currently provide?

Most post-trial care needs are not consistently facilitated by non-patient stakeholders. Major exceptions include emergency care necessary to treat side effects or device complications, routine medical care related to the instigating condition, and explantation due to medical

indications, all of which are generally covered by patients' health insurance—provided they have insurance. However, insurance coverage levels may vary based on (1) type of insurance, (2) FDA approval status for the patient's condition, (3) availability of supporting data that are sufficient to qualify for CMS coverage, (4) the ability of each patient to coordinate care, (5) the availability of additional funding mechanisms, and (6) financial resources and leadership support in the relevant professional organizations.

Currently, negotiations among stakeholders occur on a case-by-case basis (i.e., by trial, device, or patient). Post-trial plans that will be managed by the stakeholders must be established before a trial begins to reduce negotiation durations. These plans must be ethically grounded with concrete, pragmatic strategies.

What should be the minimum in continuing trial responsibilities that should be facilitated in implanted neural device trials? When would stakeholders have responsibilities to provide more than the previously defined minimum?

Discussants agreed that in any clinical trial, trial teams must prepare for post-trial care accommodations ahead of a trial's launch and must clearly communicate to patients what care access and costs to expect after the trial ends. Ideally, these teams should include clinical trial patients during the trial design process, especially while planning for post-trial care. Teams should also employ participation incentives to increase patient population diversity, which may increase the degree of financial need by patients after trial completion.

Stakeholders should ensure that any patients who experience symptomatic benefit maintain post-trial access to devices and device maintenance options, including availability of all necessary hardware updates and replacements, software updates, and any associated care. Device design by manufacturers should use interchangeable and industry-standard hardware components and should facilitate safe and easy explantation. Any patient who does not maintain access to a beneficial device for any reason should be provided with an alternate treatment.

Discussants agreed that the minimum post-trial care should include providing patients with access to both medically indicated and elective explantation. Discussants emphasized that data should be considered the property of patients from whom they were gathered rather than the researchers who gathered them, and so these data must be available to patients. All patients—those who will and will not have post-trial care access—should receive support while transitioning out of trial conditions.

Patients entitled to more than minimum post-trial care are patients who face high levels of risk, receive low levels of monetary compensation for trial participation, have limited access to alternate treatments, and/or have strong relationships with the trial team. Discussants agreed that those descriptions fit all patients in implantable neural device trials and thus all such patients are entitled to more than the minimum post-trial care.

How can gaps in post-trial patient care be closed?

Discussants agreed that the best strategies to mitigate identified gaps will be more impactful by quantifying the scale of current unmet needs. Nonetheless, discussants identified the following potential strategies to address the gaps identified during the workshop:

- Patients can consent to follow-on studies in exchange for guaranteed financial coverage of device-related health care.
- Trial teams and sponsoring organizations can provide end-of-trial documentation that informs patients of post-trial care expectations.
- Device developers, in collaboration with regulatory agencies and clinicians, can ensure that trial participants receive rapid access to approved devices.
- Funding organizations (e.g., NIH) can require that post-trial care plans be included in grant applications and can establish funding mechanisms specifically to address post-trial care needs.
- Regulatory agencies can introduce orphan device designations to encourage development of devices to treat rare conditions.
- The Centers for Medicare and Medicaid Services (CMS) can guarantee coverage of device-related care between a trial's end and FDA approval.
- Stakeholders can develop a funding strategy similar to a trust that pays for device-related health care of former trial patients.
    - Stakeholders can lobby legislative bodies for development of a fund similar to the Vaccine Injury Compensation Program that would meet this need.
- Stakeholders can include patients and patient advocates during device review processes.
- Stakeholders can advocate to legislative bodies for changes to current policies that limit coverage and reimbursement options for trial and former trial patients.
- Stakeholders can develop a registry of former implantable device trial patients.
- Stakeholders can form patient support groups consisting of former and current patients of implantable neural device trials.

Although no formal guidelines were developed, discussants agreed that this workshop served as a valuable step toward filling gaps in post-trial care.

Meeting Summary

Background

Saskia Hendriks, MD, PhD, NIH

The Neuroethics Working Group (NEWG) of the Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative held a Workshop on Continuing Trial Responsibilities on May 24-25, 2022. This workshop convened stakeholders for clinical trials of implantable neurological devices, including representatives from the National Institutes of Health (NIH), health insurers, device manufacturers, patients, caregivers, researchers, regulators, and bioethicists. Meeting participants were tasked with discussing reasonable expectations for post-trial care plans that could inform best practices for the clinical trials research community. Developing agreed upon post-trial care policies is necessary to reduce risks and burdens for patients participating in implantable device trials and to address research-related needs after initial trial completion. Currently, some BRAIN funding opportunity announcements (FOAs) require long-term care plans in funding applications, but many patients still experience difficulty in obtaining post-trial care for devices that benefit them.

Stakeholders' capacities to support patients may be limited by research goals and opportunity costs. Financial responsibilities for health care may lie with patients—provided that patients were fully informed of and consented to the post-trial needs they would experience until Food and Drug Administration (FDA) approval. However, patient needs may persist indefinitely for a number of reasons, including if a trial discontinues early, no regulatory approval is obtained, a former participant lacks coverage options, or manufacturers discontinue the product. Thus, researchers must determine how post-trial care plans can best meet the unique needs of patients and respect those patients' contributions to research.

Within the implantable neural device field, stakeholders have found broad agreement with the following three statements: (1) post-trial needs within a variety of potential scenarios should be anticipated ahead of the trial, (2) professional stakeholders have a limited, shared responsibility to facilitate continued access to devices that benefit participants, and (3) patients should be informed about post-trial needs and plans.

Panel 1: What continuing trial needs may participants have in relation to their trial participation?

Deep Brain Stimulation: An Implanted Neural Device Clinical Trial Participant's View on Post-Trial Responsibilities

Brandy Ellis, Trial Participant

Ms. Ellis lives with treatment-resistant depression and had received 25 different unsuccessful treatments before entering an open-label implantable deep brain stimulation (DBS) device clinical trial at Emory University. She believed that even if the device did not work for her, she

might benefit others by participating in a research study. The device has helped Ms. Ellis to feel well, but the recovery process required several years.

In the 11 years since enrollment, Ms. Ellis has engaged with communities of similar trial participants through social media, participated in a documentary regarding such trials, and befriended participants in her own trial who have shared concerns and suggestions for researchers to consider. Patients highlighted important post-trial challenges that are well-known before the launch of a trial, including battery replacement, lead and battery repositioning, malfunctions, the availability of rechargeable batteries, and long-term follow-up care. "Known unknown" needs that may be patient-specific or difficult to predict before trial launch include insurance coverage, access to the trial team, length of time that a device may function, a device's hackability, and device compatibility issues. Patients in Ms. Ellis's communities suggested that researchers provide further clarity on (1) when a study is no longer considered an experiment and thus may alter patients' responsibilities, (2) incentives for manufacturers to maintain device compatibility with other companies and future models, and (3) data that researchers can release to other providers to facilitate post-trial care.

Ms. Ellis suggested that patients should receive monetary incentives and guaranteed financial coverage of any post-trial care relating to the device, which can improve the socioeconomic diversity of the clinical trial patient population. Ms. Ellis further emphasized the importance of providing to patients a perpetual point of contact and a patient registry so that doctors can be aware of a patient's possession of an implanted device.

End User Subject/Trial Participant Consumer Lived Experience

Jennifer French, MBA, NeuroTech Network

Ms. French was paralyzed during a skiing accident in 1998. Her tetraplegia was successfully treated with a neural implant 18 months following her injury. She now leads NeuroTech Network, an advocacy group which has found that people participate in clinical trials for three primary reasons: (1) altruism, (2) access to new devices and treatments, and (3) personal benefit. Incorporating the lived experiences of patients within clinical trial study design is critical, particularly during early stages while defining the study objectives. Even teams performing preclinical studies should consult with people with lived experience to increase translatability to later stage trials.

While developing trial guidelines for future researchers, stakeholders must address a variety of themes, including engagement, scope, and planning; ethics embedded along the entire development spectrum; the motivation of different stakeholders; and regulatory and compliance oversight. Patient concerns regarding post-trial needs range widely from concerns regarding costs and future device care to possible adverse effects. Device-related issues include maintenance and repair, backward compatibility, upgrade eligibility, and access to consumables. Participants also express concern regarding related medical costs and long-term follow-up processes. Adverse event-related issues include loss of device function, infections, and the psychological impacts of device use. Ms. French added that she has personally experienced multiple device failures and replacements since the initial implantation.

Regulations regarding planning for post-trial care vary across agencies (e.g., FDA, NIH, the Centers for Medicare and Medicaid Services [CMS]), leading to a lack of clarity regarding responsibility for providing care. Some policy discrepancies are caused by recent changes—for example, CMS previously provided coverage for all FDA investigational devices but now conducts its own device evaluation. Standardizing these approaches may lead to the development of policies that better address patient needs.

Patient Perspectives on Post-Trial Access to Implantable Neurotechnologies

Gabriel Lázaro-Muñoz, PhD, JD, Harvard Medical School

Mr. Lazáro-Muñoz conducted a survey of patients enrolled in government and industry implantable neural device trials. This survey addressed how participants experienced consenting procedures and why they believed that different entities may hold some financial responsibility. Many patients who received experimental adaptive DBS devices do not recall having discussed ethics topics with the trial team, though these concerns would have been addressed both pre- and post-surgery, according to trial teams and consenting procedures. Patients' apparent forgetfulness may be due to their desperation for solutions to their medical conditions; thus, consenting procedures must recognize the potentially vulnerable positions in which patients find themselves.

In the survey, patients who gave unambiguous answers predominantly agreed that they should be able to keep a device after a trial ends if the device benefits their own condition, regardless of its broader effectiveness or regulatory status. Patients concurred that a variety of stakeholders, including insurance companies and manufacturers, should be jointly responsible for patient medical costs during and after a trial. They noted that device manufacturers continue to receive valuable information about their products when patients keep a device. Insurance companies do not currently pay for patient care during studies but should contribute to patient health care costs following study completion. Patients who benefit from a device may be reasonably expected to be partially responsible for costs if they can afford them. Finally, research teams should be obligated to cover any costs that cannot be financially covered by other stakeholders given their relationship with patients and their work to organize the studies.

Ensuring that Participant Study-Related Needs are Met Post-Trial Completion: Responsibilities of the Investigator

James Mahoney, PhD, West Virginia University School of Medicine

Often, patients recruited for implantable neural device trials are at risk of near-term death despite being relatively young. Successful treatments may extend these individuals' life expectancies by decades, leading to the need for post-trial care plans that extend for 50 years or more. Long-term care plans should be included in the clinical trial protocol development process, and funding organizations should require those plans to be included in grants. The responsibility for designing these plans lies with investigators, even if the plans rely on actions from multiple other stakeholders (including industry partners, insurance providers, and academic partners). These plans should enable extended follow-up, device maintenance,

hardware replacement, and side effect management. Investigators must transparently communicate post-trial plans with participants prior to trial enrollment.

Funding agencies can support investigators' role in post-trial care plans by developing funding mechanisms for supplementary proposals that focus on providing additional care or collecting data after a trial's end. In addition, agencies can encourage investigators to include secondary or exploratory aims within initial protocols to address post-trial patient support.

Discussion

Expected Follow-up Duration and Potential Hurdles

When Ms. Ellis enrolled in a clinical trial for treatment-resistant depression, the trial staff told her to expect the trial to continue until FDA approval or for 10 years because consent protocols must have a defined endpoint; the trial staff explained that she could undergo a second consent process after 10 years to continue to contribute data. The need for a 10-year reconsenting process is reasonable, given that planning for future care may encounter some challenges—over the course of decades, a patient may move, a company may cease to exist, or the quality of available care may exceed that included in the original consent form. Regardless of these challenges, patients should not be required to continue participating in a clinical trial to receive future care for a successful device.

Ms. Ellis also noted that when she initially enrolled, the follow-up timeframe sounded daunting—with her symptoms, the ability to survive for even one year felt challenging. Mr. Hajjar, who is enrolled in the same study, similarly noted that he did not consider "the future" early during his trial enrollment and has only recently (after approximately three years) begun to think about the future of his device, which has a rechargeable battery with a 15-year lifespan.

In addition, the total lifespan of a device is generally unknown at trial launch. Ms. Ellis's early batteries required yearly replacements and she has only recently received a rechargeable battery with a 10-year lifespan. Ms. French noted that her clinical trial team did not originally expect that she would have any components of the original device after 24 years.

Patient Registries

Patient discussants noted that a data registry for trial participants may benefit them. Often, trial participants' medical records contain information regarding surgeries but not the trial devices (e.g., settings). An implantable neural device trial patient registry could contain a variety of additional information, such as points of contact or how to obtain an emergency replacement device. In the event that patients face emergencies or treatment needs in remote locations, having assurances that medical providers can access these data would help promote care quality. Similar registries currently exist for some prosthetic devices.

Incentives to Device Manufacturers and Researchers

To facilitate patients receiving care in a variety of locations and to potentially reduce medical care costs, Ms. Ellis suggested that device manufacturers should receive incentives to develop

cross-compatible device components (e.g., batteries). With this approach, patients could receive a replacement battery regardless of a clinician's access to a specific manufacturer's battery.

Incentives to Participate

Patient discussants noted that current trials are often designed with the assumption that patients have an established support system and independent affluence. Both Ms. French and Ms. Ellis moved regionally to more easily participate in their trials and relied on their families' care and financial support. While Mr. Hajjar has taken on debt as a patient in his trial, he noted that this debt was worthwhile because it helped keep him alive. Nonetheless, some patients may require financial support to enable them to take leave from work, relocate, or obtain childcare in order to participate in a clinical trial.

Although no incentive was included in the treatment-resistant depression DBS trial, most (21 out of 23) contacted participants enrolled in the study. These participants were recruited through existing adaptive DBS trials.

Funding and Care Contingency Plans

Researchers must consider funding requirements for post-trial care when first developing clinical trial care plans. These plans should address potential device removal and other contingencies that apply regardless of whether the device produced life-saving or life-altering results. As an example of a successful contingency plan, Ms. French described how researchers in one study explanted a device by necessity from a patient with locked-in syndrome, but provided the patient with an alternate communication device that would allow the patient to maintain an ability to communicate with a caregiver.

Patient Involvement and Representation

Ms. Ellis commented that involving patients directly during study planning and execution will benefit patient outcomes during the clinical trial, but that patients in some trials may find requests to support trials to this degree to be burdensome or beyond their capacity. In addition, researchers and patient representatives must avoid representing the patient population as unanimous. Each patient's experience differs. Researchers must therefore consider creating a Frequently Asked Questions (FAQ) document that provides multiple patient perspectives on trial participation.

Panel 2: What do different stakeholders currently provide, and what can or could they provide in terms of continuing trial responsibilities?

Patient Care Beyond the Clinical Trial

Yagna Pathak, PhD, Abbott

The bearer of responsibility for post-trial care may differ based on the type of study, but Dr. Pathak asserted that determinations of responsibility should be based on patient need and research ethics documents from the International Ethical Guidelines for Biomedical Research

Involving Human Subjects and the Declaration of Helsinki. However, these guidance documents may be contradicted by regional reimbursement and regulatory requirements, and because each trial team reinvents its own plans, these strategies may not match the ethics outlined in those documents. In fact, no device manufacturer has its own set standard for providing post-trial care, introducing not only sponsor-specific but trial-specific variation into long-term patient support. Patients in implantable neural device trials may require long-term support due to delayed regulatory approval, device explantation due to immediate medical necessity or lack of desired outcome, or expanded access to treatment as the device proceeds through trials and approval processes. Researchers should develop plans to support patients regardless of their individual outcomes in the trial and should develop anticipatory and preventative strategies to reduce the probability of negative outcomes. Moreover, research staff should define an expected number of lifetime procedures to be conducted and outline privacy and security challenges that patients may encounter within planning and consent documents.

While many clinical trials encounter similar challenges, device trials face specific challenges of their own. For example, researchers and sponsors of these trials must consider not only hardware costs, but also the costs of hospital and physician resources. Although these costs may be high, device manufacturers should consider that if patients elect to keep their devices long-term, the team and patient will have developed a potentially life-long relationship that may enable continued data collection beyond the trial's end.

The Industry Perspective

Martha Morrell, MD, NeuroPace and Stanford University

Stakeholders share not only a burden of costs for post-trial care, but also access to benefits and opportunities. Patients may experience an improvement in their health and quality of life. Researchers fulfill their academic missions and physicians are able to help patients. Society benefits not only through gaining more knowledge and access to new treatments, but also through reductions in the costs of disability adjusted life years and life-years lost. Insurers may similarly decrease costs of treating some patient and increase profit margins and industry gains business and profit. However, financial considerations alone do not motivate even all industry stakeholder motives; altruism is a unifying motivation in this research field. For example, pharmaceutical industry staff and health insurers could have used their skills in other industries where they may have earned higher salaries.

Dr. Morrell works at NeuroPace, a small company established to develop a single implantable device, Neuropace's brain-responsive neurostimulation (RNS®) System, to treat epilepsy. NeuroPace required 16 years of work and more than $315 million in funding to bring its device to FDA approval. Large profitable companies may easily cover the cost of post-trial care for patients by using funds from other revenues, but small companies such as NeuroPace may easily become insoluble, leaving patients without financial support.

NeuroPace's experience with Lennon-Gastaut Syndrome (LGS) offers an instructive example of the post-trial care barriers such small companies may face. Recently, NIH has increased its investments in research on LGS, a rare form of epilepsy that has attracted researchers

motivated to identify a treatment solution but has not offered a sufficient commercial motivation to industry. NIH has required that research studies using implantable neural devices to treat LGS include a plan for providing post-study care. As NeuroPace attempted to find a coverage solution for patients, the company found that it could not guarantee its own long-term financial solubility and sought external funding sources. However, academic institutions and hospitals were unwilling to cover post-trial care costs, nonmedical insurers would not create a policy to support trial patients, no NIH per-patient supplement existed for post-study care, and CMS had no existing mechanism for post-study care. Ultimately, NeuroPace agreed to donate the device to trials in lieu of insurance coverage for the device and participating physicians agreed to provide device-related care for free to uninsured patients. However, hospitals did not reach a similar agreement and committed only to attempting to find free or reduced care for these patients. Thus, consenting documents clarified that patients might be responsible for costs if all other insurance options were exhausted. Now that the RNS® device has been approved, coverage concerns have shifted to studies using the device in novel indications. By exploring RNS's applicability to other indications, NeuroPace may be able to improve symptoms for many individuals.

CMS Perspective

Carl Li, MD, MPH, CMS

Manufacturers may request a National Coverage Determination when they believe that their device or treatment should receive CMS coverage. CMS addresses these requests by reviewing published evidence surrounding a potential treatment, focusing on study quality, strength, and meaningful patient-centered outcomes (which may differ based on trial type). A review that finds promising but not convincing evidence may lead to a Coverage with Evidence Development (CED) designation, which allows the device sponsor to organize a CMS-approved trial in which patients receive coverage. CMS generally does not provide coverage for a given treatment after the completion of a CED trial or for alternate indications. However, CMS will cover costs related to device malfunction or battery replacement for an individual whose initial costs during a trial were funded by CMS.

CMS generally does not perform case-by-case determinations for individual patients; one patient benefitting from a device would not receive coverage as an exception for a device that overall lacked evidentiary support. Notably, CMS generally reviews FDA-approved devices rather than novel designs, which may limit coverage for other devices that have completed a trial but not yet received FDA approval.

Insurance Perspective

Rhonda Robinson Beale, MD, United Health Group

Insurance companies typically cover the costs of routine medical care, which may include device-related care, emergency medical care related to implanted investigational devices, and any medically required explantation. To receive coverage for other types of care, insurance companies require that diagnostic and treatment technologies used must have evidence of

general efficacy, which differs from a determination of apparent benefit to an individual patient benefit. Typically, insurance companies convene expert groups to review the hierarchy of evidence, weighting meta-analyses and randomized double-blind clinical trials more heavily. Insurers often request data not only from placebo-controlled trials but also comparative studies given their need to assess potential cost differentials between the new device and existing comparators. (The National Institute for Neurological Disorders and Stroke (NINDS) offers a funding mechanism specific to comparative effectiveness studies.) Experts are also asked to consider the treatment's relative benefit—for example, a treatment for a condition with a high risk of death may receive approval for coverage even with little evidence. Off-label treatments are unlikely to receive coverage due to limited supporting evidence. Nonetheless, an insurance committee may review coverage for an individual with a treatment-resistant condition, and approval can be granted specifically to that individual.

When determining coverage, insurers assess cost benefits and cost offsets, which may differentially affect how much evidence is required to provide coverage for a technology. In the United States, health care is expensive, and only 5 to 7 percent of the population generates 82 percent of the medical costs. Reducing the costs these patients incur is of great importance to insurers, who therefore consider not only the effectiveness of a treatment, but its duration, need for repetition, long-term ramifications, and need for ongoing care.

Perspectives from Insurance Providers and Research Administrators

Shirley McCartney, PhD, Oregon Health & Science University

After a device receives FDA approval, data generated during a clinical trial is released through clinicaltrials.gov and trial patients are transitioned to an institutional standard of care protocol. If a device is not approved by FDA, the patient usually has continued access to the device but may require a replacement or removal. If the patient discontinues participation in the study or the trial team ceases its study, the patient may be referred to as a trial-abandoned patient (i.e., one who may not know how to access future care).

In Dr. McCartney's experience, academic institutions rarely profit from medical research studies and frequently lose money on these projects. However, researchers in these trials can develop significant relationships with patients. In particular, researchers involved in implantable device trials should expect to maintain proactive and continuous communication with patients about each stakeholder's responsibility for the continuation of care and costs, even if a device manufacturer or research company may cease to exist. Researchers must also consider a variety of factors that may influence care and coverage, such as local or regional laws (e.g., Oregon's prohibition on psychosurgery would prevent a depression DBS trial), a lack of community trust in health care providers, or inadequate insurance coverage. Researchers should also consider that trial-based compensation for specific purposes (e.g., travel) likely ended upon FDA approval or trial end, which may leave patients with less access to continued post-trial care. In most cases, access to supportive resources may address the other challenges that patients face.

NIH Perspective

Nick Langhals, PhD, BRAIN, NIH

NIH supports technology development activities from concept initiation through clinical trial execution. The BRAIN Initiative, which includes 10 participating institutes and centers, is one of NIH's major means of achieving this support. NIH has begun requiring long-term care plans in applications for FOAs, especially those FOAs associated with the BRAIN Initiative. These plans may include information on the following scenarios: (1) device removal at the end of the study, (2) device replacement and subsequent patient monitoring, (3) repairs to external hardware, (4) psychophysical testing and psychological monitoring, (5) access to trained clinicians who can provide ongoing coverage and lifetime hospital care, (6) the purchase of designated private health insurance specific to post-trial care needs, (7) disabling the device but not removing it, and (8) the research hospital providing care in perpetuity. To assist researchers in implementing these plans, NIH offers up to three one-year no-cost extensions—the first is provided automatically, the second requires a grant submission, and the third is provided on a case-by-case basis. Researchers may use carryover funds or supplements or may conduct long-term follow-on studies. Ultimately, while NIH can require certain elements within applications, it cannot control studies that it funds but does not perform itself. Thus, NIH is primarily relegated to an advisory role.

Discussion

Regulatory Agency Disagreements

Studies are often designed to achieve FDA approval without regard to alternative means of treatment assessment, even though each approving entity in the US health care system (e.g., CMS, FDA, private insurance) uses a different process to assess safety and effectiveness. Thus, Dr. Morrell suggested that clinical trialists should be educated on these various means of assessment so that they can plan for each possibility that could impede patient access to post-trial care (e.g., closure of manufacturing company). Simply establishing a post-trial care fund may not suffice for providing care in the event of a company's dissolution or a trial's discontinuation, especially if a device is particularly innovative and requires specialized care.

For example, the CED designation supports devices at various stages of FDA's Investigational Device Exemption (IDE) process during their early research stages. At these stages, requests for nationwide coverage may be granted with limited evidence based on clinical utility. After a CED is granted, CMS will provide coverage for the device and related routine care from then on. However, CMS and private insurance rarely account for quality-of-life improvements when making coverage decisions because disability and quality of life are often difficult to quantify.

Patient Involvement

Meeting discussants emphasized the value of considering patient perspectives when making any decisions regarding the value of a treatment, stating that treatments should be valued not only in terms of commercial opportunities but also in terms of patient outcomes. Only patients can say how treatments improve their lives. FDA has recently centered drug research on patient

desires, and other agencies and entities should employ the same approach. CMS involves patients in its Medicare Evidence Development and Coverage Advisory Committee (MEDCAC).

Panel 3: What should be the minimum in continuing trial responsibilities that should be facilitated in implanted neural device trials? When would stakeholders have responsibilities to provide more than the previously defined minimum?

Perspectives from a Caregiver, Patient Advocate, and Researcher

Tracy Dixon-Salazar, PhD, Lennox-Gastaut Syndrome Foundation

Dr. Dixon-Salazar's adult daughter, Savannah, began experiencing frequent daily seizures by 3 years old. At the age of 5, she received a diagnosis of LGS and had begun to display developmental delays. By age 18, she had presented with at least six types of seizures (recorded via EEG), experienced more than 40,000 seizures, and tried 26 therapies (all which failed to provide benefit). When she was 18, Savannah's doctors determined that a genetic mutation causing a calcium-channel overactivation disorder caused her seizures; this discovery enabled physicians to try more targeted therapies. By age 28, Savannah had lessened her medicinal requirements to 4 prescriptions, reduced her seizures by 95 percent and status epilepticus by 100 percent, and begun to improve on learning tasks. Following infection with COVID-19, Savannah's epileptic status declined again. Her story, with multiple unsuccessful therapies and symptom regressions, is typical of LGS patients, which exemplifies how desperate patients may be when they enroll in implantable neural device trials.

Given this desperation, clinician researchers should focus on patient outcomes, which requires consideration of effective communication with patients, costs, transparency, and responsible study design to enable fast and efficient health care access. Patient-perspective value frameworks can help reframe ethical considerations to align with patient needs. Study design should respond to patients' values and desires, including (1) access to equipment maintenance and upgrades, (2) greatest possible compatibility in equipment components, (3) insurance coverage for the cost of devices and care, (4) universal device standards to be shared with doctors unaffiliated with the trial, (5) patient participation incentives, (6) perpetual points of contact and prohibitions on patient abandonment, (7) clear consent processes, and (8) opportunities to connect with other patients. Patients also widely request extensive data sharing capabilities to facilitate further data mining and distributed knowledge; they generally want to access to their own data, to be able to refer to findings on their own, and to ensure that their participation in trials contributes as much as possible to reduce additional trials.

In addition to designing trials around patients, clinical trialists must ensure that they clearly explain that design to patients and their families, including (1) whether patients will have access to post-trial care—including urgent care—that they need; (2) why researchers believe that the investigational treatment is safe; (3) how well researchers expect that it works; (4) how burdensome the study will be for the patient and family in terms of time, money, and quality of

life; and (5) who will have access to the patient's data. The BRAIN Initiative has supported data sharing requirements to facilitate further research, but each patient should discuss possible options for data sharing and use; patients with stigmatized conditions may be more hesitant to have data shared and patients with more life-threatening and life-limiting conditions are generally more supportive of widespread data sharing. Dr. Dixon-Salazar emphasized the importance of facilitating patient ownership of collected data, which may require deidentification of public data.

In all patient requests, obtaining support during the process of transition out of a study and into post-study care is critical to long-term success. Building research-related care capabilities around existing care services can support a patient's transition to post-trial conditions, in which the sponsor company cannot cover all health care costs. The absence of transition plans often leaves patients without access to providers who have extensive knowledge of the patient's specific treatment plan and condition.

Planning for Post-Trial Care as a Researcher in Implantable Neural Device Trials

Patricio Riva-Posse, MD, Emory University School of Medicine

Dr. Riva-Posse is the principal investigator (PI) of the trial in which Ms. Ellis and Mr. Hajjar are enrolled, as well as the PI of other depression and suicidality treatment trials. Although initial implantation and care costs were covered by Dr. Riva-Posse's trial's partnering health care system, the trial team, like many others, is required to reimburse patients for post-trial care, particularly patients who lack insurance coverage. This reimbursement requirement became especially poignant in trials using DBS devices in younger patients. DBS devices were initially designed to treat Parkinson's disease in older patients and the lifespan of the non-rechargeable batteries was less than 18 months. This short lifespan required patients to repeatedly undergo battery replacement surgeries, which not only increased costs but also put patients at much higher risk for complications. Some patients underwent six replacement surgeries before rechargeable batteries became available. Eventually, Medicare agreed to cover these surgeries, which gave researchers leverage with which to negotiate with private insurance companies. However, many patients experienced inconsistent cost coverage—for example, patients may have had one surgery covered and the following one not. These denials of coverage occurred despite evidence showing that patients' depression symptoms worsened after batteries depleted and were not replaced. He also suggested that insurance coverage is necessary for patients and suggested that insurance—particularly public insurance—should cover continued maintenance of a device for as long as a patient benefits from the treatment.

Dr. Riva-Posse highlighted the importance of collaboration between industry and NIH-funded researchers given the two sectors' differing perspectives: industry often focuses on marketability and NIH-funded researchers focus on testing evidence-based hypotheses. Combining these approaches is a valuable means of improving studies. Moreover, researchers should consider during trial design how devices impose different requirements than medications. For example, continuing to collect data after a short trial period is critical to properly understanding the value of implantable devices: clinical trials employing DBS devices

to treat depression failed at futility assessments in early studies, but the clear benefit of these devices emerged over time. Alternatively, researchers can readjust clinical trial strategies for implantable devices by requiring a longer trial, particularly given the necessity that these devices function consistently over time.

Regardless of trial design, hardware eventually changes and evolves, which can complicate planning for future care. Dr. Riva-Posse echoed other presenters, asserting that inter-compatibility among device components (e.g., pulse generators, extension cables, intracranial leads) is a necessary alteration to current industry manufacturing.

What is Owed to Participants Following a Neural Implant Study?

Ishan Dasgupta, JD, MPH, Dana Foundation; Sara Goering, PhD, University of Washington

Mr. Dasgupta and Dr. Goering conducted a literature review that found that bioethicists broadly agree that, at minimum, clinical researchers should (1) anticipate patients' likely post-trial needs, (2) inform patients of likely post-trial experiences, and (3) ensure that patients have access to beneficial post-trial treatments. In addition, bioethicists agreed that post-trial care may include providing services to patients other than access to treatment. However, current informed consent documents vary widely and may leave patients unaware of exact expectations. Patients may also face feelings of abandonment if companies fail or if studies end based on safety or efficacy concerns despite some patients observing positive results. Mr. Dasgupta presented a partial entrustment model developed by Drs. Leah Belsky and Henry Richardson, which states that investigators and trial sponsors have greater ethical obligations, especially with regard to ancillary care, to patients with whom they have developed lasting relationships and who assume significant risks. Mr. Dasgupta suggested that this model inherently applies to implantable neural device models. Furthermore, Mr. Dasgupta asserted that additional responsibilities may arise when patients are relatively uncompensated for risks and burdens or depend on researchers for continued maintenance and use of the device.

In May 2021, Mr. Dasgupta and Dr. Goering hosted a workshop regarding post-trial care obligations in the field of neurotechnology. Attendees of this workshop agreed that implantable neural device studies are unique and that their ethics may differ from those in other research contexts. For these trials, an ethical obligation exists to provide individual patients continued access to implantable neural devices that prove beneficial to them. Expansion of patient-specific outcome measures may support these individual benefit assessments. However, the concept of benefit must be understood to encompass overall trial outcomes as well as individual clinical benefit and thus remains a complex, context-dependent consideration.

During 2018-2022, Mr. Dasgupta and Dr. Goering conducted qualitative interviews with neural device trial participants as part of an R01 grant. Interviewees broadly agreed that the minimum of research-related care should include compensation for time and effort, recognition of their contributions to the research, provision of implant-related medical care for the patient's lifetime, and continued access to and upkeep for a device that benefitted a patient. Patients also agreed that more than the minimum is necessary in the unique setting of neural implant studies. They highlighted the high time and energy burdens required from patients and close

relationships with the study team as reasons for providing more than the minimum in any neural implant study. Furthermore, patients whose care was provided only in a laboratory setting and whose devices were inert during other times noted that they may derive minimal potential clinical benefit personally, even though participation may remain life-altering.

Patients recognized that compensation must not be high enough to seem coercive, but it should be sufficient to offset the burden on patients whose desperation motivates them to enroll in a study. Compensation must also account for potential loss of disability benefits for some participants, and researchers should consider tax reporting requirements for receipt of $600 in trial compensation. NEWG Workshop participants agreed that these compensation and disability benefit rules require policy changes on a federal level.

Continued Access to Investigational Medicines as a Benchmark for Continued Access to Investigational Devices

Luann E. Van Campen, PhD, MA, EthicsMatters LLC

Dr. Van Campen presented on the approach used by the Multi-Regional Clinical Trials (MRCT) group when it determined the clinical trial responsibilities for post-trial access to investigational medicines. MRCT determined that continued access to treatment is not an unbounded ethical obligation, due to the business ethics principle of stewardship of limited resources. That principle mean that stakeholder-specific duties are dynamic, especially as a device proceeds from clinical trial to widespread availability. Sponsor responsibility is greatest during the clinical trial, whereas the government, payor, and provider responsibilities increase as broad availability increases.

MRCT determined that four guiding bioethics principles (i.e., autonomy, justice, nonmaleficence, beneficence) shape the conditions under which provision of continued access to treatment became an obligation. In particular, MRCT agreed that the duty for researchers to do no harm increases as the potential for harm from a disease increases, and thus the obligation to provide continued treatment access also increases with disease severity. The group identified seven specific boundary criteria that determine whether researchers are obligated to provide ongoing care. At the study program level, (1) the disease under study is serious or life-threatening or a research participant could be adversely impacted by treatment discontinuation, (2) no suitable therapeutic alternatives are available to participants, (3) no alternative access to the investigational product exists, (4) continued provision will not adversely affect the viability or completion of the product trials, and (5) the overall study population benefit to risk ratio is favorable. In addition, (6) the research participant receiving care must have completed the trial protocol and (7) have experienced benefit exceeding risk from the treatment.

MRCT also determined that ten variables impact the ability to provide continued treatment access to specific individuals. Some limitations arise because of challenges in distributing treatment (e.g., due to drug or device development phase, product supply, or existing mechanisms for provision), while others depend on the research team's inability to determine

an individual's benefit from the investigational drug or device (e.g., due to use of comparators during the trial, use of blinding procedures, or informed consent procedures). Most variables impact investigational devices and investigational drugs in similar ways. The primary differences between providing post-trial care for devices and for medicines are the potential stakeholders involvement, the need to consider harms of device removal, the implantable's "oneness with the body," the manufacturer and research team's relative lack of experience with the device during care transition, and the challenge of providing ongoing device support. Notably, using this framework developed to determine whether researchers in drug trials are ethically obligated to provide ongoing access to treatment suggests that researchers in device trials are nearly always ethically obligated to continue to provide ongoing care.

FDA Perspective

John Marler, MD, FDA

FDA aims in any IDE review to determine whether possible risk is balanced by possible benefit. FDA review of IDEs includes consideration of the safety of device explantation, plans for device maintenance or removal, and the consent form's description of all potential risks. FDA regulations do not specifically address downstream adverse events when devices remain implanted after trial conclusion. However, FDA guidance states that investigators should ensure that subjects "receive appropriate medical evaluation and treatment until resolution of any emergent condition related to the study intervention that develops during or after the course of their participation in a study, even if the follow-up period extends beyond the end of the study at the investigative site." FDA encourages patient-level device tracking for marketed, cleared, or approved devices.

Dr. Marler suggested several possible measures to improve trial subject privacy and health autonomy after the end of a study. He emphasized that researchers should (1) give patients a platform to share information and report experiences independently of FDA, manufacturers, and investigators; (2) design devices for safe and easy removal; (3) ensure the availability of replacement external components (e.g., controllers) that may be lost or damaged; (4) add a device identification number; (5) create an "immortal" website for devices and their design to easily produce aftermarket replacements; (6) ensure easy recognition of devices, models, and software versions; and (7) maintain a resource that identifies each patient's implanted device. Dr. Marler emphasized that researchers should anticipate problems, be transparent in consent forms, provide patients with a long-term means of implantable device identification for easier communication with future health care providers, and aim to provide more than "minimum" post-trial care—in part because aiming for ideal solutions may reveal intermediate steps. However, researchers managing a single trial will face cost limitations; when those limitations arise, the focus must first be on patient safety.

Discussion

Trial Design

Dr. John Marler noted that clinical trials can become unnecessarily complicated, resulting in patient dropout that at high rates can significantly hinder data interpretation. Thus, designing

trials with patient needs in mind benefits the trial results as much as it benefits patients themselves.

Discussants noted that trial teams may need to reassess when a trial is over, especially in the context of implantable neural devices that patients may retain for life.

Minimum Care Needs

Discussants identified several potentially necessary actions that stakeholders should take to support patients during and after a trial. Discussants agreed that implantable neural device patients are owed more than the agreed-upon minimum post-trial care provided to every clinical trial participant. Dr. Dixon-Salazar stated that prioritizing the various requests highlighted during the workshop was virtually impossible, but highlighted that researchers must make consenting processes more patient-friendly, include patients or patient advocates in trial design at various stages of treatment development, connect patients with each other to provide support systems, ensure patients have access to psychological services, and develop a transition plan for maintaining post-trial care. Dr. Chiong commented that when discussing minimum required care, discussants should consider how patients' various roles--as colleagues, patients, volunteers, or team members—affect this threshold.

Discussants also noted that current definitions of "benefit" may be too narrow, and researchers should reconsider who should define the concept. In addition, such definitions—and post-trial care in general—should be considered at the outset and design of a trial and device (e.g., safe and easy removal, compatibility). Regardless of changes to the manufacturer or study team's status, patients must maintain access to life-altering beneficial care.

Post-Trial Transition

Dr. Goering emphasized the necessity of ensuring that patients are supported while transitioning out of studies. Mr. Hajjar echoed this perspective, noting the value of Dr. Riva-Posse's responsiveness to any questions or concerns he has encountered. Dr. Dixon-Salazar suggested that a transition plan may require further discussion at a time later than initial consenting procedures. Mr. Hajjar concurred, noting that although a transition plan was discussed during his original consenting procedure, he was not in a state of mind to internalize what he was told and had to rely on his parents' support; he later contacted Dr. Riva-Posse and the study team to review what to expect during transition to post-trial care.

Dr. Riva-Posse underscored the importance of ongoing contact and consenting processes, as well as an openness to receiving questions from patients. His study team encourages patients to bring family or friends to the consenting process because the team recognizes that patients are vulnerable due to their desperation for help and their potential depression. Given Dr. Lazáro-Muñoz's survey results that most patients did not even recall discussing post-trial care in the consent process, he concurred with the importance of bringing care partners to consent procedures and stated that transitional and post-trial care discussions must be especially emphasized during the consenting process. Dr. Dixon-Salazar clarified that informed consent is important but that because current informed consent procedures are often guided by

Institutional Review Board (IRB) and FDA requirements, they are frequently not patient-friendly.

Cost

Meeting participants discussed cost considerations during health care coverage provision. For example, children with LGS receive health care coverage through government programs and nearly every LGS patient is recognized as having a long-term disability, leaving them eligible for Medicare. Meanwhile, DBS treatment for depression was first investigated in Canada, where costs posed less concern due to nationalized healthcare. Most patients in the United States who seek these depression treatments are not covered by Medicare. Dr. Lazáro-Muñoz emphasized that patients who are not capable of financing their own care must be supported by researchers or industry sponsors until another entity assumes costs.

Forum Discussion

Discussants addressed how to address gaps identified during the workshop.

Funding Organizations

When NIH awards research grants, it can review how well a device's design addresses post-trial care needs (e.g., through component interchangeability or ease of explantation). However, NIH is not able to direct researchers' practices after the funding period ends, which has a particular impact when a device manufacturer dissolves or ends support for a given device. All stakeholders must assess and mitigate risks as much as feasible, but in cases such as these, stakeholders—NIH included—cannot manage the problems identified. Ms. French noted that to plan for such issues, NIH should advocate for incorporating patients in protocol design from early research stages.

Dr. Morrell noted that requiring companies to cover patients' financial obligations may limit the types of research projects with which they engage. However, treatments for rare diseases receive financial incentives and intellectual property protections that have not yet been extended to orphan devices—pursuing an orphan disease-like program for implantable neural devices may reduce these hurdles. A similar priority for devices addressing treatment-resistant conditions may be valuable.

Transition to Approval or From Study

Dr. Greely suggested that trial participants should be eligible for more rapid access to approved devices. However, patients relying upon devices that receive FDA approval may encounter challenges in achieving care during the post-trial transition process and those whose devices ultimately do not receive FDA approval may lack access entirely. Patients whose device is no longer supported require aid during the transition to an alternate treatment.

Ms. Ellis noted that end-of-trial documentation may help support patients transitioning to post-trial care and that researchers could consider introducing new consent documentation at that time for enrollment in follow-up studies, which could be similar to registry suggestions proposed earlier during the workshop.

Patient Reimbursement

Trial design and funding should account for patients' travel expenses (e.g., supporting power wheelchair users for their specific expenses). Ms. French suggested that, in exchange for financial coverage and benefits, patients should be encouraged to participate in and share data during long-term follow-on studies to avoid loss of potential data collection.

Coverage Requirements

CMS Coverage

If an IDE is approved for coverage, CMS will generally cover the device, hospital, and surgical costs. However, Dr. Riva-Posse stated that his studies had not always been able to bill for an IDE because of a lack of billing codes. Dr. Morrell asked whether CMS could cover some portion of device-related care for trial patients after a trial ends, given the small patient population in device studies. In particular, if CMS could cover these costs between trial end and either approval or the beginning of post-approval studies, FDA's aims may be more easily met, and other insurers often follow CMS direction.

Private Coverage

Ms. Ellis commented that her private insurer can at any time decide not to cover her device-related care. If her device failed, she would need to wait for her condition to worsen, be designated as disabled and rely on Social Security Disability Insurance (SSDI) for 24 months, and only then be able to request Medicare coverage for the required maintenance. Ensuring that trial patients can access guaranteed coverage (e.g., through Medicare) would be valuable and could save her life, as well as many other lives.

Strategies for Covering Care Costs

Dr. Morrell noted that defining risks in device trials is critical. Patients not covered by insurers will face higher costs, which may influence the trial's risk assessment. In past studies, Dr. Morrell stated that the study sponsor would be the payor of last resort at a rate benchmarked to Medicare schedules. However, many institutions determined that this approach was inequitable and requested instead that patients either be insured or that the sponsor cover all costs. One inequitable aspect highlighted by these institutions is that it does not account for the copays borne by insured patients and for lifetime maximums, which patients may reach more rapidly if they encounter complications during the risky surgeries undertaken in Dr. Morrell's studies.

Developing insurance policies or allocating funds that specifically cover patients' implantable neural device trial-related health care costs following trial completion may circumvent these risks. However, most insurance companies cannot adequately estimate risk for investigational devices, and the trial population is often so small that costs remain too high for reasonable insurance coverage. An NIH fund for patient care may help trials avoid private insurance companies that would refuse to cover a pool of only high-risk patients. Some participants felt that the fund would suffer from needing to provide regular large payments without risk-dilution from lower-risk participants' contributions, but Dr. Lazáro-Muñoz suggested that this funding should be considered not as a means to dissipate risk, but instead as a pre-allocated care fund

for patients. In fact, Dr. Grady suggested that this fund could be modeled after the Vaccine Injury Compensation Program (VICP); however, VICP was developed through Congressional legislation.

Actionable Steps

To determine how best to proceed, it may be helpful for the NEWG to quantify how frequently individuals lose access to trial devices and for what reasons and must also quantify how much financial need is associated with patient care in trials. Dr. Morrell noted that FDA may have some of these data, because it requires that manufacturers record and notify FDA of all device explantations and instances where patients are contacted for recalls.

Dr. Karen Rommelfanger highlighted the formal development of interpatient support groups as a near-term goal. Intermediate-term goals may include a Congressionally Directed Medical Research Programs (CDMRP) model that employs patient advocates to review grants. Long-term goals may require that discussants address challenges with insurance policies and regulations, which requires Congressional action. Dr. Goering echoed the necessity of lobbying for changing compensation restrictions to better offset costs for patients.

Dr. Goering further suggested reviewing the nuances of individual trials to better design future studies.

Conclusion

During this Workshop, NEWG progressed toward its goal of defining post-trial care responsibilities for implantable neural device trial patients and identifying strategies to support stakeholders in meeting those responsibilities. In addition, many discussants volunteered to take ownership of future actions that support this strategizing and to develop actionable steps toward meeting those responsibilities. Dr. Ngai noted that the length of a trial period and the care inequities inherent in the United States health care system (both cost and the ability to advocate for oneself) clearly hinder current post-trial care. Not all contingencies can be addressed and no one perfect solution exists. However, some creative solutions are available, and the BRAIN Initiative considers this workshop an early step for defining and managing these longer-term approaches.

Appendix: Agenda

All times ET

DAY 1

12:00 PM Welcome
John Ngai, PhD, BRAIN, NIH

12:05 PM Introduction and Background
Saskia Hendriks, MD, PhD, NIH

12:15 PM **Panel 1: What continuing trial needs may patients have in relation to their trial participation?**

Deep Brain Stimulation: An Implanted Neural Device Clinical Trial Participant's View on Post-Trial Responsibilities
Brandy Ellis, Trial Participant

End User Subject or Trial Participant Consumer
Jennifer French, MBA, NeuroTech Network

Patient Perspectives on Post-Trial Access to Implantable Neurotechnologies
Gabriel Lázaro-Muñoz, PhD, JD, Harvard University

Ensuring that Participant Study-Related Needs are Met Post-Trial Completion
James Mahoney, PhD, West Virginia University School of Medicine

1:15 PM **Panel 1 Discussion**
Co-moderators: Winston Chiong, MD, PhD, University of California San Francisco; Nina Hsu, PhD, NINDS

1:45 PM **BREAK**

2:30 PM **Panel 2: What do different stakeholders currently provide, and can or could they provide, in terms of continuing trial responsibilities?**

Patient Care Beyond the Clinical Trial
Yanga Pathak, PhD, Abbott

Continuing Trial Responsibilities
Martha Morrell, MD, NeuroPace and Stanford University

CMS Perspective
Carl Li, MD, MPH, CMS

Insurance Perspective
Rhonda Robinson Beale, MD, United Health Group

Perspectives from Insurance Providers and Research Administrators
Shirley McCartney, PhD, Oregon Health & Science University

NIH Perspective
Nick Langhals, PhD, BRAIN, NIH

4:00 PM **Panel 2 Discussion**
Co-moderators: Sameer Sheth, MD, PhD, Baylor College of Medicine; Nina Hsu, PhD, NINDS

4:45 PM Day 1 Wrap-Up

5:00 PM Adjourn

DAY 2

12:00 PM Welcome
John Ngai, PhD, BRAIN, NIH

12:05 PM Recap of Day 1
Nina Hsu, PhD, NIH

12:30 PM **Panel 3: What should be the minimum in continuing trial responsibilities that should be facilitated in implanted neural device trials? When would stakeholders have responsibilities to provide more than the previously defined minimum?**

Perspectives from a Caregiver, Patient Advocate, and Researcher
Tracy Dixon-Salazar, PhD, Lennox-Gastaut Syndrome Foundation

Planning for Post-Trial Care as a Researcher in Implantable Neural Device Trials
Patricio Riva-Posse, MD, Emory University School of Medicine

What is Owed to Participants Following a Neural Implant Study?
Ishan Dasgupta, JD, MPH, Dana Foundation; Sara Goering, PhD, University of Washington

Continued Access to Investigational Medicines as a Benchmark for Continued Access to Investigational Devices
Luann E. Van Campen, PhD, MA, EthicsMatters LLC

FDA Perspective
John Marler, MD, FDA

1:45 PM **Panel 3 Discussion**
Co-moderators: Christine Grady, MSN, PhD, NIH Clinical Center; Saskia Hendriks, MD, PhD, NIH

2:30 PM **BREAK**

3:00 PM **Town Hall with Stakeholders**
Co-moderators: Hank Greely, JD, Stanford University; Saskia Hendriks, MD, PhD, NIH

4:30 PM Day 2 Wrap-Up

4:40 PM **Closing Remarks**
John Ngai, PhD, BRAIN, NIH

4:45 PM Adjourn