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Regulating Posttrial Access to In-Dwelling Class III Neural Devices

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19.1 INTRODUCTION

Research participants in clinical trials often have an interest in maintaining access to a drug or device after the trial has concluded. In the case of clinical trials of in-dwelling Class III medical devices, which are life-sustaining or risky devices that are implanted in the body, participants' interest in posttrial access is considerable. Such devices can be harmful to the participant if not properly maintained or removed, and if the device is beneficial to the participant, they may desire surveillance and maintenance to ensure proper device functioning, as well as access to replacement devices.

To date, the Food and Drug Administration (FDA) has not provided clear guidance about the posttrial access obligations clinical trial sponsors and investigators have to research participants. And while litigation about posttrial access in the case of investigational drugs has resulted in courts finding that there is no legal duty for pharmaceutical companies to continue to provide access to the tested drug to study participants, it is not clear how this body of law would apply to in-dwelling Class III medical devices or what normative obligations sponsors and investigators of such device trials have.

Legal and ethical clarity on this issue is of critical importance, given that such devices, unlike drugs, will remain in a participant's body and may require ongoing maintenance, surveillance, replacement, or explanation.[1] Further, prospective research participants may decline to enroll in studies assessing the safety and efficacy

[1] Saskia Hendriks et al., Ethical Challenges of Risk, Informed Consent, and Posttrial Responsibilities in Human Subject Research with Neural Devices: A Review, 76 JAMA Neurology 1506 (2019); Joseph J. Fins, Deep Brain Stimulation, Deontology and Duty: The Moral Obligation of Non-Abandonment at the Neural Interface, 6 J. Neural Eng. (2009).

of embedded Class III medical devices if they are not guaranteed posttrial access. Such recruitment problems could inhibit production of scientific knowledge and delay effective medical devices from making it to the market, thus harming innovation.

This chapter first explains the FDA approval process for Class III medical devices and the resulting issue of posttrial access to in-dwelling devices. The chapter then explores the law and ethics of posttrial access for drugs, devices, and biologics, highlighting the dearth of legal guidance. The chapter then discusses the case of posttrial access to deep brain stimulation (DBS) and patient perspectives on this issue. We conclude with a call for transparency about the type and degree of posttrial access as part of the preimplantation informed consent process as well as mandating that sponsors fund device maintenance or explantation after the conclusion of the trial.

19.2 POSTTRIAL ACCESS TO IN-DWELLING CLASS III MEDICAL DEVICES?

The FDA categorizes medical devices based on the type and degree of risk from the device. Class III medical devices, such as pacemakers or deep brain stimulation (DBS), are the highest-risk category, and thus receive more scrutiny from the FDA. Class III medical devices are defined as those that are "life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or . . . present a potential unreasonable risk of illness or injury."[2] Such devices must, through scientific evidence, demonstrate "reasonable assurance" of safety and efficacy prior to FDA approval.[3]

Not all clinical trials of Class III medical devices will successfully demonstrate safety and efficacy, necessary conditions for receiving FDA approval.[4] Other clinical trials may be successful on these measures, but the study sponsor and investigators may ultimately decide not to bring the device in question to market.[5] Both scenarios can strand research participants who may have an interest in maintaining access to the device if the intervention is or perceived to be efficacious, especially if the device is implanted in the research participant's body (also referred to as invasive or in-dwelling devices).[6] Posttrial access may include routine device maintenance, repair or replacement if the device malfunctions, or device removal, all of which often require specialized skills that only study investigators have. Uncertainty about

[2] 21 C.F.R. § 860.3(c)(3).

[3] Id. at 860.7. The Food and Drug Administration is responsible for "ensuring the safety, efficacy, and security of . . . drugs, biological products, and medical devices." Food & Drug Admin., What We Do, https://www.fda.gov/about-fda/what-we-do.

[4] Hendriks et al., supra note 1, at 1510 (demonstrating development path for neural devices).

[5] Even if the device is marketed, the manufacturer may discontinue the device. Id.

[6] "Invasive neural devices require an incision or insertion to place or implant the device in a person." Id. at 1506. See also Joseph J. Fins et al., Being Open Minded about Neuromodulation Trials: Finding Success in our "Failures," 10 Brain Stimulation 181 (2017).

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posttrial access to in-dwelling devices may dissuade prospective participants from trial enrollment, potentially thwarting the progression of device development from bench to bedside.

As the next section demonstrates, there has been little regulatory guidance from the FDA about the posttrial obligations owed to participants by device or drug sponsors and little case law clarifying this issue.[7] Furthermore, while industry norms tend to govern posttrial access to pharmaceuticals – often offering limited posttrial access[8] – these norms are neither established nor directly analogous to questions of posttrial access to in-dwelling Class III medical devices, such as DBS.

19.3 LAW OF POSTTRIAL ACCESS

Statutory and regulatory guidance for posttrial access to drugs, biologics, and devices is sparse. Most of the attention has instead focused on the passage of state and federal right-to-try laws and expanded access (i.e., compassionate use) to investigational drugs and devices through the 21st Century Cures Act.[9] Conceivably, a former study participant could seek posttrial access through one of these other routes,[10] but the legal and ethical rationales for permitting or prohibiting such access will differ. Right-to-try laws allow terminally ill patients and their physicians to request access to early-stage drug trials, although the study sponsor does not have to grant access.[11] Right-to-try laws exclude medical devices.[12] The FDA also has an expanded access program for seriously ill patients who have no other treatment options to access investigational medical products, including medical devices, that have not yet demonstrated safety or efficacy.[13]

[7] Richard S. Saver, At the End of the Clinical Trial: Does Access to Investigational Technology End as Well?, 31 W. N. Eng. L. Rev. 411 (2009).

[8] Id.; Christine Grady, The Challenge of Assuring Continued Post-Trial Access to Beneficial Treatment, 5 Yale J. Health Pol'y L. & Ethics 425 (2005).

[9] 21st Century Cures Act, Pub. L. No. 114-255, 130 Stat. 1033 (2016). See also Jordan Paradise, Three Framings of "Faster" at the FDA and the Federal Right to Try, Wake Forest J. L. & Pol'y (forthcoming).

[10] Although with the right-to-try route, they will likely be unsuccessful as industry grants very few of these requests. Paradise, supra note 9. And even if industry were to grant more requests, patients may not have the means to pay for the drugs or devices because their health insurance likely will not cover experimental medication. Id.

[11] Right to Try Act, Food, Drug, and Cosmetic Act § 561B (2018); see also Paradise, supra note 9.

[12] Only investigational drugs and biologics are included. US Food & Drug Admin., Right to Try, https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/right-try; see also Paradise, supra note 9.

[13] Id.; US Food & Drug Admin., Expanded Access for Medical Devices, https://www.fda.gov/medical-devices/investigational-device-exemption-ide/expanded-access-medical-devices. There are other pathways to access medical devices that have not demonstrated effectiveness, such as the Humanitarian Device Exemption (HDE), which permits patients with rare diseases to access medical devices meant to benefit them. Food & Drug Admin., Humanitarian Device Exemption, https://www.fda.gov/medical-devices/premarket-submissions/humanitarian-device-exemption. The

While accessing investigational drugs and devices outside of enrollment in a clinical trial may be possible through right-to-try laws and expanded access FDA pathways, these options do not directly address the situation of someone who formerly had access to an investigational drug because of their participation in a safety or efficacy study and desires continued access. Moreover, if the device has already made it to market, the expanded access pathway is no longer relevant.

Case law provides some insight into the responsibilities study sponsors and investigators have to provide posttrial access to pharmaceuticals to clinical trial participants. In the mid-2000s, in two well-known court cases,[14] participants in a study testing a new drug for Parkinson's disease wanted continued access to the drugs that they believed were beneficial, but the study sponsor ended the trial because there were safety concerns and limited evidence of efficacy. The study sponsor also refused to provide posttrial access even under the compassionate use option.[15] The study participants argued that there was a contractual duty for the sponsor to provide posttrial access, that they relied on the sponsor's promise to provide the drugs post trial, and that the study sponsor had a fiduciary duty to participants that required posttrial access.[16] Their breach of contract claim failed because the agreement study participants had was with investigators (i.e., the informed consent document) rather than the study sponsors; their promissory estoppel claim failed because again, there was no promise made by the study sponsor to study participants; and the breach of fiduciary duty claim failed because the court declined to find the study sponsor to be a fiduciary, or a person who is expected to act in the best interest of another. The court also considered policy reasons for providing posttrial access, namely that patient enrollment will decline if this is not ensured, but also considered policy reasons against a mandate for sponsors to provide posttrial access, namely that companies would be less inclined to sponsor drug trials in the future.

Posttrial access continues to be governed by private agreement rather than public regulation,[17] which means that study participants are only entitled to what study

HDE pathway to medical devices has unintended negative consequences for scientific advancement because persons requesting access to the device may not enroll in clinical trials assessing the devices' efficacy. Joseph J. Fins et al., Neuropsychiatric Deep Brain Stimulation Research and the Misuse of the Humanitarian Device Exemption, 30 Health Aff. 302 (2011).

[14] Abney v. Amgen, Inc., 443 F.3d 540 (6th Cir. 2006); Suthers v. Amgen, Inc., 441 F. Supp. 2d 478 (S.D. N.Y. 2006); see also Saver, supra note 7 (describing these cases); Michelle M. Mello & Steven Joffe, Compact versus Contract – Industry Sponsors' Obligations to Their Research Subjects, 356 N. Eng. J. Med. 2737 (2007) (describing these cases); Vinion v. Amgen Inc., 272 Fed.Appx. 582 (9th Cir. 2008).

[15] The study participants argued that the study sponsor was motivated by financial concerns rather than safety and efficacy concerns.

[16] The Vinion cases argued for breach of contract, but also various tort claims such as "negligence, misrepresentation, and infliction of emotional distress," all of which failed.

[17] See Hendriks et al., supra note 1, at 1511 (describing this in the case of clinical trials for invasive neural devices); Emily Underwood, Researchers Grapple with the Ethics of Testing Brain Implants, Science Magazine (Oct. 31, 2017), https://www.sciencemag.org/news/2017/10/researchers-grapple-ethics-testing-brain-implants.

sponsors and investigators are willing to explicitly agree to, which may not accord with participant preferences or ethical principles such as benevolence, nonmaleficence, and justice. For example, prior to one study of DBS for severe depression, the study sponsor, a medical device company, agreed to pay for the surgery to remove the device and continue supplying batteries.[18] While many participants reported experiencing a benefit from the device, the trial was unsuccessful, and participants who wished to retain the device were left to cover the costs of future maintenance and care themselves, a situation that raised many ethical issues.[19] Given the absence of legal guidance, ethical practice becomes more important. The next section addresses normative dimensions of posttrial access.

19.4 ETHICS OF POSTTRIAL ACCESS

There has been extensive academic commentary about what, if any, ethical duties are owed to clinical trial research participants. Multiple commentators have argued that if participants have experienced a benefit from an investigational intervention during a trial, the principles of nonmaleficence and beneficence demand that they should continue to have access after the trial concludes.[20] Similar arguments for access to trial benefits using the principle of reciprocity have been made given that participants have undergone risk to advance scientific understanding and benefit future patients.[21] These two arguments are embedded in an earlier version of the Declaration of Helsinki, adopted by the World Medical Association: "[a]t the conclusion of the study, patients entered into the study are entitled ... to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits."[22] Finally, some have argued in the case of DBS trials, the principle of nonabandonment brings with it "a longitudinal fiduciary obligation to provide [research participants] with support," specifically "a responsibility to provide on-going care and a fiscal responsibility for any associated costs" on the part of study investigators and sponsors.[23]

Some argue that determinations about posttrial access should be left to the discretion of investigators and sponsors because there may be uncertainty about whether there is true efficacy of the intervention or whether the benefits outweigh the harms for individual clinical trial participants and for the population at large.[24]

[18] Underwood, supra note 17.

[19] Id.

[20] Grady, supra note 8; Saver, supra note 7; Tom L. Beauchamp & James F. Childress, Principles of Biomedical Ethics (7th ed. 2013).

[21] Grady, supra note 8; Saver, supra note 7; Beauchamp & Childress, supra note 20.

[22] WMA Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects (1964), https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/; see also Grady, supra note 8; Saver, supra note 7.

[23] Fins, supra note 1, at 2.

[24] Beauchamp & Childress, supra note 20; Saver, supra note 7. Courts have also addressed the concern that requiring posttrial access may "deter pharmaceutical companies from sponsoring clinical trials as

Some also contend that research participants may have already received benefits from study participation, addressing reciprocity obligations.[25] Offsetting this argument in the case of Class III devices, any benefits may also be accompanied by potential burdens or complications associated with in-dwelling devices or their removal.[26] Furthermore, while participants likely expect posttrial access to the investigatory technology in part because of a therapeutic misconception,[27] the appropriate remedy to this problem is not posttrial access.[28] Instead, scholars have generally called for greater planning and transparency about posttrial access.[29] Finally, mandating posttrial access may raise research costs, ultimately disincentivizing research, resulting in collective societal harm.[30]

While scholars have engaged in the above-described debates, there have been many fewer studies of the viewpoints of participants about duties owed to them stemming from trial participation, especially in the context of in-dwelling devices. Existing empirical research of clinical trial participant attitudes about duties owed to them by investigators, research sponsors, drug and device manufacturers, and regulators has found that many, although not all, participants think there is a duty to provide posttrial access to a drug (or its equivalent) that provided them with benefits after the trial and until approval,[31] and after approval at a fair market or reduced price, for an indefinite period of time.[32] This small body of empirical research about posttrial expectations focused on reports from drug trial participants. It is unknown how device trial participants view these questions.

19.5 DEEP BRAIN STIMULATION AND POSTTRIAL ACCESS

Posttrial access to DBS, which is classified by the FDA as a Class III medical device[33] because it has a greater level of risk to patients,[34] is a particularly pressing issue. DBS is a "programmable and adjustable implant of electrodes into specific deep brain structures that delivers electrical impulses to alter circuit function and overcome

clinical trial sponsors might be required to continue to produce and distribute a drug they believed to be dangerous." Abney v. Amgen, Inc., 443 F.3d 540, 553 (6th Cir. 2006).

25 Saver, supra note 7.

26 Fins, supra note 1.

27 Paul S. Appelbaum et al., The Therapeutic Misconception: Informed Consent in Psychiatric Research, 5 Int'l J. L. & Psychiatry 319 (1982).

28 Saver, supra note 7.

29 Id.; Mello & Joffe, supra note 14.

30 Grady, supra note 8; Saver, supra note 7.

31 This period of time can be lengthy. Grady, supra note 8.

32 Neema Sofaer et al., Subjects' Views of Obligations to Ensure Post-Trial Access to Drugs, Care, and Information: Qualitative Results from the Experiences of Participants in Clinical Trials (epic) Study, 35 J. Med. Ethics 183 (2009).

33 21 C.F.R. § 882.

34 See Hendriks et al., supra note 1, at 1507–8 (describing risks from invasive neural devices, including risks from the surgery to implant the device, risks from the device itself, adverse side effects, privacy and security risks, and financial risks).

abnormal activity."[35] Once properly implanted, the electrodes can be stimulated with varying levels of voltage to produce desired cognitive, emotional, and physical effects. A battery for the electrodes is placed in a patient or research participant's chest. DBS has been shown to be effective and is approved by the FDA for Parkinson's disease[36] and has been tested for treatment-resistant neuropsychological disorders, such as depression.[37] The application of DBS for traumatic brain injuries is currently being explored.[38]

While all research participants have interests in posttrial access to investigational drugs or devices, the stakes are higher for persons enrolled in trials of invasive Class III medical devices, such as DBS, given the higher level of risk of the device coupled with the reality that participants cannot remove the devices. So unlike in clinical drug trials in which the participant can discontinue use of the study drug after the conclusion of the trial, participants in in-dwelling medical device trials have a device permanently embedded, barring a procedure to remove it.[39] Participants in such trials thus have a pressing interest in the device's safety, and if efficacious, ensuring that it remains available to them. This is especially the case for invasive neural technologies. Not only do implanted neural devices share the features of risk and permanence of other in-dwelling medical devices such as cardiac pacemakers, but they affect the brain, and implicate cognitive abilities, personality, identity, and agency in a way that other investigational devices and drugs may not,[40] which again raises the stakes of posttrial access.

Because both electrodes and the battery are implanted devices that cannot be removed by the participant, questions arise about how these devices will be surveilled, maintained, replaced, or removed after the clinical trial assessing their safety and efficacy concludes, especially if the device never receives FDA approval, never makes it to the market, or the device manufacturer stops making the device.[41]

[35] Id. at 1507.

[36] Günther Deuschl et al., A Randomized Trial of Deep Brain Stimulation for Parkinson's Disease, 355 N. Eng. J. Med. 896 (2006); Hendriks et al., supra note 1, at 1507.

[37] See, e.g., Helen S. Mayberg et al., Deep Brain Stimulation for Treatment-Resistant Depression, 45 Neuron 651 (2005); see also Hendriks et al., supra note 1, at 1507 (describing state of DBS research applications).

[38] Nicholas D. Schiff et al., Behavioral Improvements with Thalamic Stimulation after Severe Traumatic Brain Injury, 448 Nature 600 (2007); Hendriks et al., supra note 1, at 1507; Central Thalamic Stimulation for Traumatic Brain Injury, 1UH3 NS095554-01, PI Schiff.

[39] Devices may have to be removed if there is an infection subsequent to implantation, a complication that occurs for about 5 percent of patients who undergo DBS, or for other complications such as device malfunctioning or lead migration. Onanong Jitkritsadakul et al., Systematic Review of Hardware-Related Complications of Deep Brain Stimulation: Do New Indications Pose an Increased Risk?, 10 Brain Stimulation 697 (2017). There may also be infections from battery placement or replacement. Jonathan Dennis Carlson et al., Deep Brain Stimulation Generator Replacement in End-Stage Parkinson Disease, 128 World Neurosurgery 683 (2019).

[40] Hendriks et al., supra note 1, at 1511. Investigational drugs that target neuropsychiatric disorders may also implicate similar issues of identity and agency.

[41] Id. at 1510 (depicting lifecycle of device from the start of a clinical trial).

Indeed, there are significant hardware risks with DBS "including infection, malfunction, erosion, and migration or fracture of leads, which may require additional surgery or explantation."[42] Furthermore, many persons implanted with DBS need access to specialized neurosurgeons and neurologists for battery replacement and device programming, which they may not have access to once the study concludes.[43] Even if DBS research participants have continued access to study investigators, "they may be left with costs for device maintenance, continued access, or explantation,"[44] which often are not budgeted for in grants that fund this research and which health insurance likely will not cover.[45] As one of us asked over a decade ago when writing about research participants in trials of investigational neuromodulation technology, "What is their fate? What happens to these patients when the trial ends? Who provides on-going care? Who pays for battery replacement? Who removes a broken device? Who adjusts stimulation parameters . . . in perpetuity?"[46]

Recent ethical guidance from the NIH BRAIN Initiative Neuroethics Working Group, of which one of us (JJF) is a member, about posttrial access to neural devices such as DBS addresses some of these questions. The guidance includes the following recommendations: planning in advance of a study for research participants' posttrial access needs, regardless of whether the device is safe and effective, including planning for cost; ensuring that posttrial access issues are addressed in the process of obtaining institutional review board approval for the study and that plans are communicated to research participants in the informed consent process; and requiring greater obligations posttrial from study sponsors and investigators if the device is beneficial or risky, the study participants are vulnerable, the provision of access would not be costly, the device is too complex for general health care professionals to manage, or the device contains "built-in obsolescence and proprietary hardware and software, effectively locking patients and clinicians into ongoing relationships with a manufacturer."[47]

While the Working Group offered ethical guidance about posttrial access to neural devices, their suggestions do not have the force of law and it is unclear to what extent study sponsors and investigators are heeding these suggestions. Indeed, the Working Group notes that the "locus of posttrial responsibilities is currently determined on a case-by-case basis."[48] And importantly, the views of research

[42] Id. at 1507.

[43] Fins, supra note 1, at 2 (describing the problem and arguing that engineers should make simpler devices that primary care physicians could operate and create better, longer-lasting batteries).

[44] Hendriks, supra note 1, at 1508.

[45] Id. at 1511. MedPac, An Overview of the Medical Device Industry, in Report to the Congress: Medicare and the Healthcare Delivery System 220 (2017), http://www.medpac.gov/docs/default-source/reports/jun17_ch7.pdf?sfvrsn=0.

[46] Fins, supra note 1, at 2.

[47] Hendriks et al., supra note 1, at 1511. Because many medical devices are modified slightly from earlier versions, the lifecycle of a typical device is less than two years. MedPac, supra note 45, at 211.

[48] Hendriks et al., supra note 1, at 1511.

participants enrolled in clinical trials of invasive neural devices such as DBS regarding posttrial access remain unclear.[49]

Presently, as part of an ongoing larger study, we are studying the perspectives and experiences of research participants in a DBS clinical trial for patients with moderate to severe traumatic brain injury,[50] and one question we ask is about participants' concerns about posttrial access to the investigational device.[51] Preliminary results from research participants provide a window into the posttrial access hopes and concerns of those enrolled in invasive neural device clinical trials.

Study participants have questions and concerns about posttrial access. Some participants ask about device support and maintenance prior to agreeing to participate in the trial. One participant described proactively engaging their health insurer to determine whether their insurance policy would cover the cost of battery replacement, for example, and also asking investigators about the length and degree of posttrial support. While he understood budgetary constraints of guaranteeing posttrial access in perpetuity, he thought that if there was a benefit from the device, participants should have ongoing access to support and maintenance.

Another study participant became concerned about posttrial access after they had already been implanted. The participant indicated a desire that the device be turned up, and that it never be turned off because it provided such a benefit. The study participant did not want to go back to a time when the device was not available. In fact, the participant emphasized that future study enrollees be warned that they may have a negative experience if their device is turned off during or after the study because they will revert to their old self. That is, if participants experience a beneficial change due to DBS, then if they no longer have access to a functioning device (e.g., dead batteries, faulty electrodes, etc.), they may feel harmed. This participant's informal caregiver also echoed the study participant's concerns, emphasizing that the positive effect of DBS on the participant's life has been so profound that they hoped that the device is never turned off.[52]

[49] Some research has shown that "patients receiving DBS expect researchers to provide posttrial medical care, expertise, and equipment (batteries)." Id. at 1510.

[50] Cognitive Restoration: Neuroethics and Disability Rights, 1RF1MH12378-01, PI Fins; Central Thalamic Stimulation for Traumatic Brain Injury, 1 UH# NS095554-01, PI Schiff; Nicholas D. Schiff et al., Central Thalamic Brain Stimulation Modulates Executive Function and Fatigue in a Patient with Severe to Moderate Traumatic Brain Injury, Annual BRAIN Initiative Investigators Meeting (Apr. 13, 2019).

[51] Research on participants' views on invasive investigative medical devices is in its infancy, but some qualitative research on participants enrolled in DBS for depression and OCD trials indicates that participants need DBS adjustments fairly often and also need access to battery maintenance, which implicate posttrial access issues. Eran Klein et al., Brain-Computer Interface-Based Control of Closed Loop Brain Stimulation: Attitudes and Ethical Considerations, 3 Brain-Computer Interfaces 140 (2016).

[52] The study participant also expressed concern about changing the battery or knowing whether the device was programmed correctly.

While more data about the views of participants and their informal caregivers is needed, these preliminary insights speak to the need to hear the voices of those most proximate to these trials. As we continue our study, we plan to add more research participant perspectives to the policy and ethical debate over posttrial access to implanted Class III medical devices.

19.6 ADAPTING THE REGULATORY REGIME FOR INNOVATIVE MEDICAL DEVICE TECHNOLOGIES

The FDA recently released draft guidance calling for patient input into clinical trial design for medical devices.[53] The guidance about patient engagement is meant to "mitigate some of the practical challenges to robust clinical investigations, including challenges concerning study/research participant enrollment and retention in the study" through strengthening the informed consent documents and prioritizing clinical endpoints patients care about, for example.[54] Another important part of patient feedback on clinical trial design is what patients/participants and families think investigator and sponsor responsibilities are with respect to posttrial access to a functioning embedded medical device. These data can help inform policy creation.

As data collected from participants in our study has shown, individuals have an interest in maintaining access to a safe and effective device after their participation in a clinical trial ends. But while their perspectives are important, they are just one part of the regulatory puzzle. The views of investigators, sponsors, and manufacturers also need be considered, as the social compact centering around device implantation transcends the narrow purview of informed consent, especially if there are conflicts between participant preferences and the sponsors or manufacturers bringing innovative devices to market given economic constraints.

We argue for a bifurcated conception of responsibility for posttrial access. With respect to investigators, we argue, that at a minimum, they owe a duty of complete transparency to participants and prospective participants about posttrial access to surveillance, maintenance, upgrades, or removal of Class III implanted devices as part of an ongoing informed consent process. Transparency about posttrial access necessitates advance planning. Our argument for planning and transparency is in

[53] US Food & Drug Admin., Patient Engagement in the Design and Conduct of Medical Device Clinical Investigations: Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders (2019), https://www.fda.gov/media/130917/download. This guidance accords with the view that creating policy based in part on participant/patient preferences will increase welfare. Mark A. Hall et al., Rethinking Health Law, 41 Wake Forest L. Rev. 341 (2006); Lois Shepherd & Mark A. Hall, Patient-Centered Health Law and Ethics, 45 Wake Forest L. Rev. 1429 (2010).

[54] US Food & Drug Admin., supra note 53. A participant/patient-centered approach also enhances compliance and facilitates embodiment of devices by the participant. Eran Klein et al., Engineering the Brain: Ethical Issues and the Introduction of Neural Devices, 45 Hastings Ctr. Rep. 26 (2015).

line with the recommendations from the NIH BRAIN Initiative Neuroethics Working Group discussed previously.[55]

Duties to plan for and be transparent about posttrial access are not limited to medical device trials. Indeed, these duties apply to all clinical trials, including pharmaceutical trials, because disclosing posttrial access plans to prospective participants is necessary to obtain genuine informed consent. But ensuring ethical clinical trials of Class III implanted devices, especially neural devices, demands more of investigators and sponsors to ensure that study participants are not harmed and are treated justly, given participants' posttrial access preferences and expectations; the greater risk to study participants, many of whom are vulnerable because of their existing medical conditions, from implanting a device; the probable permanence of the device and the need for ongoing access to specialized medical care and device maintenance; and the potential for changed personality and identity with a brain-based medical intervention.

Thus, with respect to study sponsors and the medical device industry, we argue that there is a correlative set of responsibilities to participants and their families to ensure ongoing access to repairs, maintenance, and the costs of explantation (should participants desire device removal) for embedded neural devices. Funds should be put aside at the start of a trial to ensure such access after a trial has concluded. While this requirement may seem financially onerous, these costs would likely be a small fraction of the total expenditures related to research and device development. Indeed, these ongoing costs should be understood as central to maintaining the integrity of this work, as part of the cost of doing business, and a concrete set of ethical obligations given the unique challenges of in-dwelling neural devices.[56] With this recommendation, we move beyond what the NIH BRAIN Initiative Neuroethics Working Group proposes, given the many qualifications contained in their arguments about posttrial access (e.g., conditioning investigator and sponsor responsibility to provide access on criteria such as study participant vulnerability, degree of device benefit, cost of posttrial access, etc.).[57]

These additional responsibilities should be more than an ethical duty – they should also be legally required. But unlike the current norm of leaving matters of posttrial access to private agreements, we argue that posttrial access decisions

[55] Hendriks et al., supra note 1.

[56] Ensuring posttrial access to implanted neural devices can be considered a "compensatory ethic," which weighs the needs and preferences of study participants over those of investigators and sponsors given the risk the participant has borne and the undesirability of potential benefits only accruing to others if the participant is not ensured posttrial access. See Joseph J. Fins, Pandemics, Protocols, and the Plague of Athens: Insights from Thucydides, 50 Hastings Ctr. Rep. 50 (2020) (describing the compensatory ethic with respect to ventilator allocation guidelines and preference given to health care providers given their service at great risk in the context of the COVID-19 crisis).

[57] Hendriks et al., supra note 1.

should be subject to regulatory oversight by the FDA, which can ensure that investigators and sponsors are fulfilling their ethical duties to study participants after balancing the competing interests, if any, of the parties. Additionally, both aspects of this bifurcated set of responsibilities should be approved by an Institutional Review Board prior to the beginning of the clinical trial.[58]

[58] See also Fins, supra note 1, at 2.

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