Pediatric and congenital electrophysiology society initiative on device needs in pediatric electrophysiology

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Introduction

There are few cardiovascular devices approved in children (Table 1), with only 5 devices approved for use in the pediatric electrophysiology patient in the last 10 years. This lack of appropriate pediatric-tested technology has resulted in a high rate of off-label device utilization in children.[1] Sutherell et al[2] found an off-label use of an approved device in 63% of patients treated in an interventional pediatric cardiology program.

Although off-label use of devices may be warranted in many pediatric cases, it raises significant concerns as devices are being used in scenarios for which they have not been tested. These devices may not perform in the same manner or with similar predictability or reliability in pediatric and congenital heart disease (CHD) patients as they do in adult patients, for whom they were initially developed and evaluated. Pediatric patients have faster underlying heart rhythms, have smaller cardiac structures, and place additional stresses on devices resulting from physical activity. Additionally, these device therapies may be required for significantly longer periods of time compared to the older adults for which they were often intended.

The regulatory approval process of the Food and Drug Administration (FDA) includes an evaluation of the available data to establish a reasonable assurance of safety and

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Table 1 Cardiovascular medical devices approved by the FDA for pediatric application 2008–2018

Device	Generic description	Year	Mechanism of approval
NeuRX RA/4 Respiratory Stimulation System	Diaphragm pacing stimulator	2008	HDE
Helios II Diagnostic Ablation Catheter	**Cardiac ablation catheter**	**2009**	**PMA**
Repel-CV Bioresorbable Adhesion Barrier	Bioresorbable adhesion barrier	2009	PMA
Melody Transcatheter Pulmonary Valve and Medtronic Ensemble Transcatheter Valve and Delivery System	Prosthetic percutaneous pulmonary valve	2010	HDE
RX Acculink Carotid Stent System	Carotid stent	2011	PMA
Medtronic Vascular Endurant Stent Graft System	Endovascular stent	2011	PMA
Valiant Thoracic Stent Graft System	Endovascular stent	2011	PMA
RX Herculink Elite Renal Stent System	Renal stent	2011	PMA
Legoo	Temporary vessel occluder	2011	PMA
TAXUS Express2 Paclitaxel-Eluting Coronary Stent System	Drug-eluting coronary stent system	2012	PMA
AXUS Liberte Paclitaxel-Eluting Coronary Stent System	Drug-eluting coronary stent system	2012	PMA
ION Paclitaxel-Eluting Coronary Stent System	Drug-eluting coronary stent system	2012	PMA
Berlin Heart EXCOR Pediatric Ventricular Assist Device	Ventricular assist device	2012	HDE
VALIANT THORACIC STENT GRAFT	Endovascular graft	2013	PMA
Melody Transcatheter Pulmonary Valve, Ensemble Transcatheter Valve Delivery System	Percutaneous pulmonary valve	2015	PMA
Impella RP System	Right ventricular assist device	2016	HDE
LifeVest Wearable Defibrillator	**Wearable defibrillator**	**2016**	**PMA**
The Edwards SAPIEN XT Transcatheter Heart Valve (THV)	Percutaneous aortic valve	2016	PMA
Blazer Open-Irrigated Ablation Catheter	**Cardiac ablation catheter**	**2016**	**PMA**
EXCOR Pediatric Ventricular Assist Device	Ventricular assist device	2017	PMA
AED Plus—Zoll	**Defibrillator**	**2017**	**PMA**
HeartSine Samaritan PAD 350P	**Defibrillator**	**2017**	**PMA**
Melody Transcatheter Pulmonary Valve (TPV) and Ensemble Transcatheter Valve Delivery System	Transcatheter pulmonary valve	2017	PMA
AMPLATZER PFO Occluder	Percutaneous PFO occluder	2017	PMA

Bold indicates EP/arrhythmia devices.
HDE = humanitarian device exemption; PFO = patent foramen ovale; PMA = premarket approval.

effectiveness, or safety and probable benefit in the case of humanitarian use devices receiving a humanitarian device exemption, prior to marketing approval. Data may include, but is not limited to bench testing, animal studies, clinical data, and real-world evidence. Although the premarket data review provides important information regarding a device's safety and effectiveness, new safety concerns may emerge once a device is on the market. The FDA has various programs that facilitate post-market monitoring of device performance, including voluntary reporting by manufacturers, health professionals and consumers. However, these methods have limitations. A key limitation is that there is insufficient data to assess the total population (ie, the denominator) in which the device is being used. Additionally, there is no current method for organizing adverse event reports and distributing them to the health care providers using these devices in an off-label manner in children. Sporadic reports of pediatric-specific events are published by industry-clinician collaborations, but these are relatively rare compared to large adult studies.[3] Reporting of adverse events associated with off-label use may be lacking, which may compromise opportunities to optimize device use in these respective populations.

There are limited data available concerning device safety and effectiveness in pediatric and CHD populations. Pediatric congenital cardiac patients may be exposed to implanted devices for long periods of time. However, they typically represent a small number of device patients overall, which makes large randomized trials more challenging.[4] When considering return on investment, there may be limited financial incentive for companies to invest in the development of pediatric medical devices, especially considering that pediatric patients commonly represent less than 1% of the market for a device.[4]

In the past 5 years, there have been several initiatives in pediatric cardiology, specifically in the heart failure and interventional cardiology domains, to develop and market devices that have been designed for the pediatric patient.[5,6] The Pediatric and Congenital Electrophysiology Society (PACES), the international organization representing pediatric and CHD arrhythmia specialists, developed a task force in 2016 to specifically address comprehensive device development issues for the pediatric/CHD arrhythmia patient, ranging from cardiovascular implantable electronic devices (CIEDs) to ablation catheters. PACES is an international society for pediatric electrophysiology (EP) specialists and encompasses the majority of pediatric electrophysiologists in the United States. The PACES task force mission is to develop a collaborative relationship between care providers, industry and FDA to facilitate development in pediatric electrophysiology. It aims to advance the outcomes of pediatric patients with electrophysiologic disease by improving the range of available diagnostic and therapeutic devices.

The FDA is dedicated to advancing public health and seeks collaborative opportunities to support development of medical devices that serve the complex needs of children. It has engaged pediatric specialists to better understand and prioritize device needs within their specialties and have supported these physicians in engaging industry representatives. Additionally, the FDA has been developing innovative and least-burdensome approaches to enhance care options for pediatric populations while maintaining evidentiary standards.

In November 2016, a PACES task force, supported by the Heart Rhythm Society, met with representatives from the FDA Center for Devices and Radiologic Health (CDRH) to discuss the present state of medical device technology as it relates to the needs in the congenital electrophysiology area. FDA leadership confirmed the intention of the FDA to work with all stakeholders, including academia and industry, to support development in the pediatric medical device ecosystem. The PACES task force clarified priority medical device development opportunities (outlined below) aimed at enhancing care options for children with arrhythmias.

In May 2017, members of the PACES task force, FDA and industry met to discuss these issues and to share expertise in pediatric needs, development challenges, and regulatory requirements. This document reviews those issues, including specific pediatric needs and existing obstacles to development of pediatric-specific technology, and identifies opportunities to address these issues.

Specific pediatric/adult congenital heart disease issues

Hemodynamic and physiological differences

Moderate to severe congenital heart disease requiring therapy affects 6 in 1000 live births in the United States.[7] Cumulative survival estimates for this population have increased from 25% in the 1960s to >90% expected survival to adulthood in the current era.[8] Tachyarrhythmias and bradyarrhythmias are common sequelae of congenital heart disease palliation, and often require intervention in the form of implantable pacemakers, implantable cardioverter defibrillators (ICDs), cardiac resynchronization therapy (CRT) devices, or catheter ablation therapy.

These diseases are often characterized by limited access to intracardiac structures, morphologic intra-cardiac changes and endocardial and epicardial scarring. CHD such as congenitally corrected transposition of the great arteries or Ebstein anomaly of the tricuspid valve can present with anatomic issues that can complicate implantation of a cardiac implantable electronic device (CIED). Intracardiac shunting may prohibit a transvenous approach in a CIED secondary to the increased risk of thromboembolism gaining access to the systemic circulation. This may necessitate use of an epicardial device.[9] Venous access may be an issue in patients who have required multiple devices in the past.

Other issues when considering device therapy in children include patient size, longevity and physiologic heart rate ranges. The vasculature in infants through preschoolers is often too small to accommodate a 7 Fr ablation catheter or a transvenous ICD lead. At present in the United States, there is only a single 5 Fr ablation catheter available for use in the smallest of patients. Small patients often require ICD leads placed in non-traditional manners in the subcutaneous, pericardial or thoracic space.[10,11] These novel ICD configurations are associated with a higher lead failure rate compared to conventional ICD lead placement (49% vs 76% system survival at 3 years; $P < .01$).[11] Throughout childhood and adolescence, children will exhibit different growth rates. Over the first 2 years of life, children will usually grow 11 to 14 inches. During adolescence, a child will grow several inches over a 4- to 6-month time period. These growth spurts can make lead management a challenge. Both transvenous and epicardial leads are placed in pediatric patients with redundant lead to accommodate growth, but this redundancy can be limited by current patient size and anatomy, as well as fibrosis and other limiters to lead length.

Pediatric patients are likely to outlive the expected longevity of their current CIED and lead, which exposes them to potentially complex and risky lead extraction procedures and the need for multiple device and lead replacements. Increased pacing rates due to higher intrinsic heart rates in pediatric patients also result in shorter battery life and more frequent generator changes. Rate responsive algorithms that were designed for adult criteria are typically not adequate for the normal physiologic response to exercise seen in children, who tend to have faster heart rate rise and recovery than adults.[12] Nonstandard generator locations, such as the abdomen, were not studied when designing accelerometer-guided rate-response and excluded from clinical trials, such that data are not available. Similarly, the software algorithms designed to fine-tune the pacing and defibrillation characteristics of pacemakers and ICDs have not been validated in clinical studies of children or patients with CHD.

Higher physiologic heart rhythms can also result in inappropriate discharges in pediatric patients with ICDs. This partly explains the higher inappropriate ICD discharge rate compared to adult patients. Other etiologies of inappropriate discharges

Table 2 PACES/FDA/industry initiatives

Challenges	Initiatives	Time line
Education	Semi-annual meeting of PACES representatives, FDA industry, patient advocates, payers	Short-term
	Standing pediatric advisory board for all device companies, of experts in pediatric electrophysiology, overseen by PACES	Short-term
Lack of available data	Development of pediatric consortium to allow for gathering of pediatric and CHD specific data	Long-term
	Continued pediatric enrollment in IMPACT for pediatric EP studies (and soon for pacemakers and ICDs)	Short-term
Financial issues	Development of pediatric consortium with emphasis on improving cost-effectiveness	Long-term
	Discussions on national level regarding changes in ICD-10 coding and tax incentives	Long-term

CHD = congenital heart disease; EP = electrophysiology; FDA = Food and Drug Administration; ICD = implantable cardioverter–defibrillator; PACES = Pediatric and Congenital Electrophysiology Society.

include abnormal T waves (often seen in hypertrophic cardiomyopathy and inherited arrhythmia patients) resulting in double counting of the heart rate, sinus tachycardia, and lead failure secondary to somatic growth.

Technical issues

There is considerable momentum toward miniaturization of all medical devices to allow for home use (such as in a ventricular assist device) and lower power consumption. Smaller devices are critical in the pediatric population in which the smallest patients may be 1–2 kg. However, there may be unanticipated challenges associated with device miniaturization. The Sprint Fidelis lead experience is a good example of unanticipated issues associated with smaller leads in younger patients. The Sprint Fidelis was a small (6.6Fr) ICD lead developed by Medtronic and released in 2004. Soon after its release, a higher than expected failure rate was identified, which eventually led to a recall of the lead in 2007.[13] Several retrospective studies revealed that younger patients with better systolic function and higher physical activity were at the highest risk of lead failure.[14–16] Thus, the patients thought to be most suitable for a small lead were also those at highest risk.

Regulatory issues

The majority of high-risk medical devices, those that may support or sustain human life, proceed along the Premarket Approval (PMA) regulatory pathway to achieve FDA approval. The PMA pathway requires demonstration of both safety and effectiveness as judged by the FDA. Typically, this is accomplished through one or more randomized clinical trials. This requirement is most suitable for relatively common diseases and is often impractical in low-volume pediatric diseases, for which population and potential market size may limit the options for conducting and financing clinical trials.

The FDA is cognizant of the regulatory obstacles that complicate device approval in a disease process that affects only a small number of patients and has taken several steps to mitigate these issues. The Humanitarian Device Exemption (HDE) pathway was developed for devices that are intended to treat a condition that affects no more than 8000 patients in the United States per year. This pathway does not require demonstration of a reasonable assurance of effectiveness but rather probable benefit. Additionally, information needs to be provided to determine that the device does not pose a significant/unreasonable risk of illness or injury and that probable benefit outweighs the risk of injury/illness. This pathway may be appropriate for devices treating congenital heart disease. This pathway often requires a clinical study to achieve this determination, without large randomized double-blinded study design. On occasion, a single arm clinical study with historical controls may be sufficient. Several pediatric cardiac devices have been approved through this pathway, including the Berlin Heart EXCOR ventricular assist device and the Medtronic Melody Transcatheter Pulmonary Valve.[5,6] To date, no pediatric-specific arrhythmia devices have been approved utilizing this pathway.

Furthermore, the FDA has been working on strengthening and streamlining the process of testing complex medical devices to ensure that clinical trials are conducted in a safe, efficient and cost-effective manner. The agency has engaged innovative new strategies to address the challenges in the pediatric population. There is considerable emphasis on utilization of available data either from retrospective studies, clinical registries, historical off-label usage and other real-world evidence.[17] In 2007, legislation was developed that allowed the use of postmarket data registries such as IMPACT and PEDIMACS to help characterize the risk-benefit profile of off-label use of devices. Alternate trial design strategies are also being considered, such as the use of propensity matched controls or performance goals.

Specific needs relevant to pediatric and congenital heart disease populations

With the backdrop of the above issues, the PACES task force was constituted in early 2016. This group was tasked to assess the present state of device therapy in pediatric and CHD electrophysiology practice and to identify possible areas of need. The initial goal was to form a working partnership with the FDA and industry to further assess each of the possible projects, characterize existing barriers and seek solutions to these barriers to enable development of therapies. Three examples of these areas of need identified by the PACES task force are illustrated below.

Ablation catheters—Cryoablation

Catheter-based cryoablation has been approved for use in cardiac ablation by the FDA since 2003. There are currently

3 different single point cryoablation catheters approved for use: a 4-mm tip, 6-mm tip and 8-mm tip. For the 4-mm tip catheter, there are two ablation modes available, controlled by temperature regulating software in the cryoablation console. A "cryomapping" mode cools the tip of the catheter to −30°C and a "cryoablation" mode cools the tip of the catheter to −70°C. When used in cryomapping mode, the cryoablation catheter cools but does not permanently eliminate function of conducting tissue in the targeted area, creating a reversible electrical effect. This allows for precise site testing and confirmation of an appropriate location prior to proceeding with a definitive cryoablation, which is performed at −70°C. The advantage of cryomapping is that the lesion can be stopped if any undesired effect is seen because the effect is temporary. Using this setting, the cooled tissue will re-warm without any permanent damage. This may reduce the occurrence of AV block, a major complication that can occur during an ablation procedure and may require implantation of a permanent pacemaker. In a historical series, some degree of AV block occurred in about 1.2% of pediatric radiofrequency ablation procedures.[18] Although this likely overstates the current prevalence of AV block during ablation, protection of the AV node remains a primary safety concern in all pediatric ablation procedures. In addition, other safety concerns, including damage to nearby coronary arteries, can be mitigated by use of cryomapping prior to definitive cryoablation. Cryomapping is currently commercially available in Europe and Canada for use with the 4mm and 6mm tip catheters and has been used safely and effectively in children.[19,20] However, only the 4-mm catheter allows for the cryomapping functionality despite the very frequent use of the 6mm tip catheter in many pediatric ablation procedures in the United States.

Cardiovascular implantable electrical devices (CIEDs)—Subcutaneous ICDs

Pediatric patients with ICDs have a higher complication rate when compared to adult patients with ICDs.[21] Newer registry data are capturing some implant and complication data in pediatric and CHD patients, although it is not mandated.[22,23] Multiple studies have shown that children have a higher incidence of inappropriate ICD discharges (ranging from 21%–25%) than adults (13% in MADIT-II).[24–27] There have been multiple explanations proposed for this discrepancy, including a higher incidence of atrial arrhythmias in children and higher sinus rates overlapping with tachycardia detection criteria.[28] A number of cardiac diseases, including cardiac channelopathies such as long QT syndrome and structural heart diseases such as hypertrophic cardiomyopathy, are more common in children with implanted ICDs and can also result in problematic electrogram (EGM) discrimination analyses. Novel ICD technology such as the subcutaneous ICD (S-ICD) offers considerable theoretical advantages in children and young adults, but studies have shown a higher rate of inappropriate discharges in the younger population.[11,21,29,30] The deficiencies in existing treatments are thus related both to inadequate device software algorithms as well as to issues related to obtaining suitable electrical vectors (hardware size match to patient). At birth, the ECG of an infant is markedly different than that of an adult. There are differences in the QRS axis, size and shape; T-wave morphology; normal resting heart rate; and cardiac intervals (PR interval, QT interval) in children when compared to adults. These variations can potentially change the efficacy of an algorithm that is based on an adult ECG tracing when applied to a child or adolescent.

Multiple algorithms have been employed by ICD manufacturers to correctly diagnose atrial and ventricular arrhythmias, but these have not been tested in children. A large set of atrial and ventricular electrograms have already been collected by the pediatric electrophysiology community from appropriate and inappropriate ICD discharges in children. In addition, pediatric electrophysiologists routinely gather atrial and ventricular electrograms during EP studies. Together, these collected electrograms could be used to develop an "arrhythmia library" and "test" proprietary algorithm performance in a "virtual" patient setting. For the S-ICD platform, sensing vectors can be simulated by placement of 3 ECG electrodes on the patient's skin at locations that represent the subcutaneous position of the S-ICD's implanted electrode. Digitized intracardiac EGM and surface ECG recordings obtained during EP studies can subsequently be processed for S-ICD analysis through a manufacturer-supplied simulator system for rhythm adjudication.[31,32]

There are some limitations to this approach. Stored electrograms from implanted devices are highly filtered and already processed. Although this is not likely to be an issue for the evaluation of simple timing-based algorithms, it may problematic for the evaluation of any algorithms that use EGM morphology. Further work to potentially evaluate device-specific algorithms may be necessary in the future.

CIED—Leadless and epicardial pacing leads

Although leadless pacemakers have logical appeal for children, their use is limited by the large diameter of vascular access and the concern for long-term device abandonment in the heart for many decades. Epicardial pacing systems are commonly used in children as well as adults with CHD secondary to small patient size, intracardiac shunts, and/or absence of systemic venous access to the chamber requiring pacing.[33,34] In patients with prior cardiac surgeries for CHD, large areas of the epicardium are often covered with dense scar tissue and adhesions with resultant difficulty in obtaining optimal epicardial lead placement to capture the myocardium at low energy thresholds. The introduction of steroid elution in epicardial pacing leads has improved lead performance by conferring lower energy thresholds in short- and long-term follow-up in comparison to non–steroid-eluting pacing leads.[35,36]

The currently available steroid-eluting epicardial pacing lead is a button-type design with a passive fixation mechanism, requiring sutures to anchor the electrode(s) to the

epicardium (eg, Medtronic 4968, 4965 models). This particular lead design works well on healthy or minimally scarred myocardium but may not be suitable for implantation in patients with densely scarred myocardium, as the electrodes do not make sufficient contact with excitable myocardial tissue. In the presence of thick epicardial scarring, an active fixation lead has a significant advantage over the passive fixation lead by achieving greater myocardial penetration and bypassing the layer of fibrosis in the epicardium. Unfortunately, currently available active fixation epicardial leads do not have steroid elution (eg, Medtronic 5071). The ideal epicardial pacing lead design for CHD patients with excessive myocardial scarring might incorporate both an active fixation mechanism as well as steroid elution. Literature showed that an epicardial pacing lead prototype (MyoDex 1084T) incorporating both of these features is marketed, but is not available in the USA. The European Commission approved the use of MyoDex in the European Union in 2005. This prototype could be useful for the increasing number of children and adults with CHD who require lifelong pacing.

Conclusion and next steps

There is a need in the pediatric electrophysiology population for medical devices specifically geared toward the pediatric and congenital cardiac patient. In response to this need, the PACES task force, members of the FDA, and industry convened to initiate discussion of key priorities.

Several important issues were raised during these discussions. First, there is a need for education and sharing of perspectives across clinicians, the FDA and industry. Pediatric electrophysiologists need to educate industry regarding the specific needs of their patient population, and how modifications to existing devices, which may already be used widely off-label in children, can influence pediatric care. The FDA needs to continue its education efforts on all the potential pathways available to industry to achieve pediatric labeling. Industry needs to share technologies in the pipeline with pediatric experts and FDA to take into consideration the most vulnerable patients who might benefit the most from new technology.

Second, expansion of FDA approval of devices has been hampered by a lack of available data in children and CHD patients. The FDA is working to facilitate the use of post-market data from national registries such as IMPACT and INTERMACS, to help assess risk–benefit profiles in devices that are currently used in pediatric and CHD patients but have not been approved in these populations.

Finally, the financial implications of either expanding indications for devices or development of new devices specifically for pediatrics are daunting. Pediatric patients are an extremely small share of the overall business of medical devices companies, and the costs associated with both development and pre-market testing are substantial, particularly in comparison to the size of the potential market. Creative financial incentives including different ICD-10 codes for pediatric devices or specific tax credits for companies embarking on pediatric devices are questions that will need to be addressed on a national level.

Effective multi-stakeholder collaboration offers the opportunity to improve device availability and potentially improve patient outcomes. The ongoing shared commitment to these efforts is essential to its continued success. We strongly support and endorse ongoing dialogue among patients, providers, payers, industry, the FDA, and other interested stakeholders in order to identify and engage opportunities where device development for pediatric and congenital electrophysiology patients might be successfully undertaken.

We suggest three possible means of achieving this goal (Table 2). First, an annual or semi-annual meeting of members of the pediatric EP community, the FDA, industry, patient advocates and payers could be useful in several ways. This group could educate each other on patient needs, industry challenges and regulatory opportunities. “Easy wins” such as gathering data on device therapy presently being used outside of the United States or minor changes to existing therapy could further pediatric device availability. Second, minor modifications in the development of new devices could make them more pediatric and congenital heart disease friendly. Pediatric electrophysiologists may be best suited to understand the relevant clinical nuances of such modifications. Therefore, we suggest a standing pediatric advisory board consisting of pediatric electrophysiologists, convened and facilitated by the pediatric electrophysiology community, be available to device companies to represent the pediatric and congenital electrophysiology population in device development. Finally, a consortium of centers willing to participate in either retrospective gathering of data, prospective registry participation, or prospective trials in a cooperative manner could make gathering of pediatric specific data more manageable and economical.

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Appendix Table A1 Writing group author disclosure table

Writing group	Employment	Consultant/advisory board/ honoraria	Speakers' bureau	Research grant	Fellowship support	Equity interests/ stock options	Other
Anne M. Dubin, MD, FHRS	Lucile Packard Children's Hospital at Stanford, Stanford University	1: I-ACT	None	None	3: Abbott; 3: Medtronic	None	1: UpToDate royalties
Bryan C. Cannon, MD, FHRS	Mayo Clinic	None	None	None	None	None	None
Elizabeth V. Saarel, MD, FHRS	Cleveland Clinic	None	None	None	None	None	None
John K. Triedman, MD, FHRS	Boston Children's Hospital, Harvard University	None	None	None	None	None	1: Biosense Webster, non-CME training; 2: UpToDate royalties
Charles I. Berul, MD, FHRS	Children's National Medical Center, George Washington University	None	None	5: Medtronic	None	0: PeriCor LLC	
Yaniv Bar-Cohen, MD, FHRS	Children's Hospital, Los Angeles, University of Southern California	None	None	None	None	None	0: Patent
Maully J. Shah, MBBS, FHRS	Children's Hospital of Philadelphia, University of Pennsylvania	None	1: Medtronic	None	3: Medtronic	None	None
Jessica Paulsen, BS	U.S. Food and Drug Administration	None	None	None	None	None	None
Hetal Patel, MS	U.S. Food and Drug Administration	None	None	None	None	None	None
Jonathan Reich, MD	U.S. Food and Drug Administration	None	None	None	None	None	None
Mark D. Carlson, MD, FHRS	Abbott	None	None	None	None	5: Abbott	5: Abbott (employment)
Kenneth Stein, MD, FHRS	Boston Scientific	None	None	None	None	5: Boston Scientific	5: Boston Scientific (employment)
James O. Gilkerson, DVM	Boston Scientific	None	None	None	None		5: Boston Scientific (employment)
Robert C. Kowal, MD, PhD, FHRS	Medtronic	None	None	None	None	3: Medtronic	5: Medtronic (employment)
Vasum Peiris, MD, MPH	U.S. Food and Drug Administration	None	None	None	None	None	None

Number value: 0 = $0; 1 = ≤$10,000; 2 = >$10,000 to ≤$25,000; 3 = >$25,000 to ≤$50,000; 4 = >$50,000 to ≤$100,000; 5 = >$100,000.