Report to Congress

Device Pilot Projects

Submitted Pursuant to
Section 708 of the FDA Reauthorization Act of 2017

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Executive Summary

Section 708 of the FDA Reauthorization Act of 2017 (FDARA) amended section 519 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360i). FDARA requires the Secretary of Health and Human Services to provide a report to the Committee on Energy and Commerce of the U.S. House of Representatives and to the Committee on Health, Education, Labor and Pensions of the U.S. Senate containing a description of the pilot projects being conducted and the pilot projects being continued or expanded pursuant to section 708 of FDARA. This is the second annual report by the Food and Drug Administration (FDA) to fulfill this requirement.

FDARA calls for, among other things, pilot projects to be designed to efficiently generate reliable and timely safety and active surveillance data. Active surveillance of medical devices may be understood relative to traditional or "passive surveillance," whereby an active approach relies on users to proactively notify FDA of device-related events (e.g., through adverse event reporting). For the pilot projects, *active surveillance* refers to actively and continuously generating information on device performance and clinical outcomes associated with device use in routine clinical practice. Active surveillance has the potential to empower stakeholders to make more timely evidence-based decisions.

The pilot projects that were initiated as required by section 708 of FDARA were designed and conducted in coordination with a comprehensive system for evaluating medical device technology. That system is the National Evaluation System for health Technology (NEST). The NEST Coordinating Center (NESTcc) operates under a governing board with appropriate representation of stakeholders, including patient groups and device manufacturers, as set forth in the law. In coordination with FDA, the NESTcc promotes the use of electronic health data, including claims data, electronic health records (EHRs), patient survey data, registries, and other health information.

The Center for Devices and Radiological Health at FDA has documented an increase in the use of real-world evidence (RWE) to support regulatory decision-making. The use of RWE in studies may be less burdensome for manufacturers because RWE is often less costly and can generate meaningful information about the safety and effectiveness of devices in a more timely manner than traditional studies.

FDARA specifies that this report should describe 1) how such pilot projects are being implemented through a contract, cooperative agreement, grant, or other appropriate agreement; 2) the number of manufacturers that have agreed to participate in such projects; 3) the data sources used to conduct such pilot projects; 4) the devices or device categories involved in the pilot projects; 5) the number of patients involved in such projects; and 6) the findings of each project in relation to device safety, including adverse events, malfunctions, and other safety information. This information is presented in the report and summarized in the Appendix.

The pilot projects reported here are at various stages of development and include several device types. Data sources are both national and state-based, and they include EHRs, registries, and claims. Devices studied include orthopedic joint implants, implantable cardioverter defibrillators, transcatheter heart valves, peripheral vascular implants, urogynecological mesh, robotic-assisted

devices, and ventral hernia mesh.

Several of these pilot projects are already producing RWE for device evaluation (premarket and postmarket) by various stakeholders, including FDA and industry. In addition, these projects will help inform the development of active surveillance and practical applications of active surveillance in real-world settings. These efforts are important to the further development of NEST and other RWE capabilities, and the future work outlined here will increase the scale and impact of these capabilities.

Contents

Acronyms Used in This Report

ACC	American College of Cardiology
AHSQC	Americas Hernia Society Quality Collaborative
AJRR	American Joint Replacement Registry
CDRH	Center for Devices and Radiological Health
CI	Confidence Interval
CRN	Coordinated Registry Network
CRT	Cardiac Re-Synchronization Therapy
DCB	Drug Coated Balloon
DES	Drug-eluting Stent
DELTA	Data Extraction and Longitudinal Trend Analysis
EHR	Electronic Health Record
EP PASSION	Electrophysiology Predictable and Sustainable Implementation Of National Registries
FDA	Food and Drug Administration
FDARA	FDA Reauthorization Act of 2017
FORCE TJR Registry	Function and Outcomes Research for Comparative Effectiveness in Total Joint Replacement Registry
ICD	Implantable Cardioverter Defibrillator
ICOR	International Consortium of Orthopedic Registries
KP	Kaiser Permanente
MARCQI	Michigan Arthroplasty Registry Collaborative Quality Initiative
MDEpiNet	Medical Device Epidemiology Network
MDR	Medical Device Reporting
NCDR	National Cardiovascular Data Registry
NEST	National Evaluation System for health Technology
NESTcc	National Evaluation System for health Technology Coordinating Center
OME	Oral Morphine Equivalents
Ortho CRN	Orthopedics Coordinated Registry Network
PAD	Peripheral Artery Disease
PAS	Postapproval Study
PCORTF	Patient-centered Outcomes Research Trust Fund
POP	Pelvic Organ Prolapse
PTX	Paclitaxel
RARC	Robot Assisted Radical Cystectomy
ORC	Open Radical Cystectomy
RWD	Real-world Data
RWE	Real-world Evidence
SEER Program	Surveillance, Epidemiology, and End Results Program
SPARCS	Statewide Planning and Research Cooperative System
SPARED	Study of Prostate Ablation Related Energy Devices
STS	Society of Thoracic Surgeons
SUI	Stress Urinary Incontinence
SVS	Society of Vascular Surgeons

TVT	Transcatheter Valve Therapy
TAVR	Transcatheter Aortic Valve Replacement
TKA	Total Knee Arthroplasty
THA	Total Hip Arthroplasty
TJR	Total Joint Replacement
VISION	Vascular Implants Surveillance Intervention and Outcomes Network
VQI	Vascular Quality Initiative

I. Purpose

Section 708 of the FDA Reauthorization Act of 2017 (FDARA) amended section 519 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360i). FDARA requires the Secretary of Health and Human Services to provide a report to the Committee on Energy and Commerce of the U.S. House of Representatives and the Committee on Health, Education, Labor and Pensions of the U.S. Senate containing a description of the pilot projects being conducted and the pilot projects being continued or expanded, pursuant to section 708 of FDARA.

II. Background on Section 708

Section 708 of FDARA calls for, among other things, pilot projects to be designed to efficiently generate reliable and timely safety and active surveillance data. Active surveillance of medical devices may be understood relative to traditional or "passive surveillance," whereby an active approach relies on users to proactively notify the Food and Drug Administration (FDA) of device-related events (e.g., though adverse event reporting). For the pilot projects, ***active surveillance*** refers to actively and continuously generating information on device performance and clinical outcomes associated with device use in routine clinical practice. Active surveillance has the potential to empower stakeholders to make more timely evidence-based decisions.

Some of the ways FDA uses active surveillance strategies for monitoring medical device safety include:

- Conducting ongoing systematic monitoring of an existing high-quality granular data source with regular feedback regarding safety alerts delivered to the manufacturer and regulators.

- Collecting postmarket safety information as evidenced in real-world data (RWD) sources (typically electronic health records (EHRs) or registry data sources), extending to monitoring the overall performance of medical devices, including the efficacy and durability of them.

- Requiring a pre-defined algorithm to detect potential safety signal detection instead of data mining or ad-hoc queries of existing data sources.

The pilot projects were designed and conducted in coordination with a comprehensive system for evaluating medical device technology as specified by FDARA. That comprehensive system is the National Evaluation System for health Technology (NEST). The NEST Coordinating Center (NESTcc) operates under a governing board with appropriate representation of multiple stakeholders, including patient groups and device manufacturers. In coordination with FDA, the NESTcc promotes the use of real-world electronic health data, including claims data, patient survey data, EHRs, registry data, and other digital health information. The Medical Device Epidemiology Network (MDEpiNet) is one of the NEST data partners and is primarily involved in advancing the Coordinated Registry Networks (CRNs) featured in the pilot studies.

As intended by the law, this report has been prepared to contribute to the independent third-party evaluation of the strengths, limitations, and appropriate uses of evidence collected pursuant to real-world evidence (RWE) pilot projects of the Medical Device User Fee Amendments of 2017, authorized as part of FDARA.

The law calls for the voluntary participation by device manufacturers in these pilot projects. Accordingly, all the pilot projects reported here are voluntary. These pilots involve the use of multiple different RWD sources.

The Center for Devices and Radiological Health at FDA has documented an increase in the use of RWE to support regulatory decision-making. The use of RWE in studies may be less burdensome for manufacturers because RWE is often less costly and can generate meaningful information about the safety and effectiveness of devices in a more timely manner than traditional studies.

III. Selection of Pilot Projects

The selection of pilot projects described in this report was guided by the law's requirement that such projects inform the development of methods, systems, data criteria, and programs that could be used to support safety and active surveillance activities for devices. The devices and device types in these pilot projects are widely used, and failure of any of these device types may be associated with significant health consequences. The pilot projects involve devices and device types for which the collection and analysis of RWE regarding the device's safety and effectiveness, therefore, is likely to advance public health.

The pilot projects reported here are at various stages of development and include several device types. Data sources are both national- and state-based, and they include EHRs, registries, and claims. Devices studied include orthopedic joint implants, implantable cardioverter defibrillators (ICDs), transcatheter heart valves, peripheral vascular implants, urogynecological mesh, robotic-assisted devices, and ventral hernia mesh.

Several of these projects are already producing RWE for device evaluation (premarket and postmarket) by various stakeholders, including FDA and industry. In addition, these projects provide tools and methods for the development of active surveillance and practical applications of active surveillance in real-world settings. These efforts are important to the further development of NEST and other RWE capabilities, and the future work outlined here will increase the scale and impact of these capabilities.

All pilot projects comply with the requirements with respect to security measures to maintain confidentiality and privacy referred to in the law.

The persons or organizations conducting these pilot projects have high levels of research, statistical, epidemiologic, or clinical capability and expertise to conduct and complete the

activities. As applicable, pilot projects are conducted under contracts, cooperative agreements, grants, or similar arrangements in compliance with all U.S. laws and regulations.

IV. Description of the Pilot Projects

FDARA specifies that this report must describe 1) how such pilot projects are being implemented through a contract, cooperative agreement, grant, or other appropriate agreement; 2) the number of manufacturers that have agreed to participate in such projects; 3) the data sources used to conduct such pilot projects; 4) the devices or device categories involved in the pilot projects; 5) the number of patients involved in such projects; and 6) the findings of each project in relation to device safety, including adverse events, malfunctions, and other safety information. Each pilot project is described herein by providing the following information:

- Pilot project name
- Description and devices involved
- Party conducting the pilot project
- Agreement type (e.g., contract, cooperative agreement, grant)
- Specific aim(s)
- Data source(s) involved
- Safety outcome(s) of interest
- Numbers and names of manufacturers involved
- Number of patients
- Findings of project
- Status (as of October 2019)

The manufacturer's involvement is broadly defined and inclusive. Some of the projects have a financial contribution from one or more device manufacturers while others do not. Additionally, some of the projects have industry representation on an oversight committee; other projects are in the process of forming those committees.

A narrative describing each pilot project is found in sections V and VI of this report. The narrative descriptions are followed by a short description of the status of each pilot project. The descriptions of the pilot projects are also summarized in the Appendix of this document.

Section V presents the findings from completed pilot projects (including three completed pilots that were listed as potential pilots in the last report), section VI provides updates for ongoing pilot projects, and section VII presents the pilot projects that were initiated in 2019. Two pilots,[1, 2] detailed in the last report, were discontinued due a lack of funding and registry stakeholder support. The details for those two pilots appear in the Appendix.

[1] Data Extraction and Longitudinal Trend Analysis (DELTA) in Transcatheter Aortic Valve Replacement (TAVR).

[2] Women's Health Technology CRN – Uro-Gynecological Mesh and Risk of Cancer.

A note about CRNs, which are frequently mentioned: Typically, CRNs are registry-based RWD sources that are linked to other sources, such as claims or EHRs, to enable studies of long-term outcomes via longitudinal patient healthcare profiles.

V. Completed Pilot Projects

1. Project name: Signal detection: Opioid use and risk of joint revision surgery

Description:

Prolonged opioid use following total knee arthroplasty (TKA) and total hip arthroplasty (THA) has not been extensively studied. Whether prolonged opioid use is a possible indicator of early arthroplasty failure was explored. Retrospective cohort studies were conducted of TKAs and THAs registered in a total joint replacement (TJR) registry from January 2008 to December 2011.

Opioid use during the first year after surgery was the exposure of interest and cumulative daily oral morphine equivalent (OME) amounts were calculated. Total postsurgical OME per 90-day exposure periods were categorized into quartiles. The end-point was aseptic revision surgery. Survival analyses were conducted, and hazard ratios were adjusted for age, gender, prior analgesic use, opioid-related comorbidities, and chronic pain diagnoses.

Party conducting the pilot project and agreement type:

The TKA pilot project was conducted by Kaiser Permanente (KP) under a cooperative agreement with FDA. The THA pilot was conducted by KP with no outside funding.

Specific aim(s):

The specific aims of the pilot projects were to determine if opioid use is associated with an increased risk of total joint revision surgery and whether this use can serve as an early signal in active postmarket surveillance of devices.

Data source(s):

The data sources for this project were KP’s TJR Registry and KP's EHRs.

Safety outcome(s) of interest:

The outcome of interest was the risk of revision surgery.

Numbers and names of manufacturers involved:

Three manufacturers were represented on the pilot advisory committee: Johnson & Johnson, Smith & Nephew, and Zimmer Biomet.

Number of patients:

A total of 24,105 TKA patients and a total of 12,895 THA patients were studied.

Findings of project:

A two-phased approach was originally under consideration for this pilot; however, the investigators completed the pilot work within the first phase publishing on the proof of concept for this methodology. The findings from the project are summarized below.

TKA findings:

The findings of this project have been published.[3] After the initial 90-day postoperative period, 41.5 percent (N = 9,914) continued to use opioids. The revision rate was 0.6 percent within 1 year and 1.6 percent within 5 years. OME use was categorized as medium-low (100-219 milligrams (mg)), medium-high (220-533 mg), and high (2: 534 mg). Compared to patients not taking any opioids, patients using medium-low to high amounts of OME after the initial 90-day period had a higher adjusted risk of 1-year revision, ranging from a hazard ratio equal to 2.4 (95 percent confidence interval (CI), 1.3- 4.5) to a hazard ratio equal to 33 (95 percent CI, 10-110), depending on the OME and time period.

THA findings:

The findings of this project have been published.[4] After the first 90 days, 27 percent continued to use opioids. The revision rate was 0.9 percent within 1 year and 1.7 percent within 5 years. Use of medium-low, medium-high, and high amounts of OMEs in days 91 to 180 after surgery was associated with 6 times (95 percent CI: 3-15), 5 times (CI: 2-13), and 11 times (CI: 3-44) higher adjusted risk of 1-year revision, respectively. The use of medium-low and medium-high amounts of OMEs in days 181 to 270 after surgery was associated with 17 times (CI: 6-44) and 14 times (95 percent CI: 4-46) higher adjusted risk of 1-year revision. There was a similar higher risk of 5- year revision.

Persistent postoperative use of opioids was associated with higher rates of revision surgery in both cohorts, and this use may be an early indicator of potential surgical failures.

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[3] Namba RS, Inacio MCS, Pratt NL, Graves SE, Roughead EE, Paxton E. Persistent Opioid Use Following Total Knee Arthroplasty: A Signal for Close Surveillance. J Arthroplasty. 2018 Feb;33(2):33 l-336. Epub 2017 Sep 13.

[4] Namba RS, Inacio MCS, Pratt NL, et al. Postoperative opioid use as an early indication of total hip arthroplasty failure. Acta Orthopaedica. 2016;87(Suppl 1):37-43.

2. Project name: DELTA-ICD leads

The Data Extraction and Longitudinal Trend Analysis (DELTA) system is designed to provide automated active safety surveillance of clinical data (EHR or registry) used to monitor the performance of marketed medical devices, medications, or other therapeutic interventions. The system is compatible with a broad array of potential data sources and supports a variety of statistical methods, allowing for both unadjusted and risk-adjusted safety monitoring for prospective and retrospective analyses.

Description:

Over the past few years, there have been several examples of high-energy ICD leads that have experienced mechanical failures at rates significantly higher than would have been predicted based on premarket testing. These events have led to several voluntary device recalls and complex clinical decisions for patients and electrophysiologists regarding the best strategies for managing patients with ICD leads. To improve the efficiency of identifying potential safety concerns with implantable medical devices, the DELTA surveillance system was developed to monitor ongoing clinical datasets to detect emerging differences in device safety (or effectiveness), including ICD leads.

Party conducting the pilot project and agreement type:

The pilot project was conducted by Lahey Hospital and Medical Center and by the Tufts University School of Medicine under a cooperative agreement with FDA and a grant from the William M. Wood Foundation.

Specific aim(s):

This pilot project validated a strategy for automated active safety surveillance of contemporary high-energy ICD leads based on prospective, propensity-matched survival analyses.

Data source(s):

The data source for this project was the ICD Registry in the American College of Cardiology's (ACC's) National Cardiovascular Data Registry (NCDR). Existing DELTA server/software installed at the ACC was used for the analyses.

Safety outcome(s) of interest:

The freedom from failure was the key outcome of interest in this study. Proposed analyses were performed using definitions provided by the NCDR to maximize the consistency of outcome and clinical covariate definitions.

Numbers and names of manufacturers involved:

These devices were produced by four companies: Guidant/Boston Scientific, Medtronic, Sorin Group, and St. Jude Medical. Manufacturers were not involved in this study.

Number of patients:

The pilot project included almost all ICDs implanted in the United States. After approval of the study protocol, and before any case-level ICD Registry data were made available to DELTA, the study was registered on ClinicalTrials.gov, and the protocol was made available through the DELTA research website. All analyses specified in the final protocol were considered "pre-specified." Findings anticipated for the pilot included the relative safety of several ICD leads which have, to FDA's knowledge, not previously been analyzed using comparative safety techniques.

Findings of project:

Among the 374,132 patients who received a new ICD implant, no safety alerts were triggered for the primary safety endpoint of lead failure for any of the high-energy leads studied. Estimated rates of freedom from lead failure at 5 years ranged from 97.7 percent to 98.9 percent for the four high-energy leads of interest. Though limited by incomplete long-term outcomes, the active surveillance of the ICD Registry suggests that there were no clinically meaningful differences in the rate of ICD survival for the four most commonly used high-energy ICD leads.

Status:

A manuscript has been submitted for publication in a peer-reviewed journal.

VI. Completed Pilots Listed as Potential Pilots in the Last FDA Annual Report

The following three projects were described within the previous report as a potential pilot project within a CRN in the process of being established. Since the last report, these projects were developed into full pilots and reached completion within a year.

3. Project name: A population-based study of ureter enteric strictures after open and robot-assisted radical cystectomy (Study of Prostate Ablation Related Energy Devices (SPARED) CRN)

Description:

The devices involved in this project were robotic devices used for assistance during radical cystectomy. There had been a growing use of robot-assisted radical cystectomy (RARC) for treating bladder cancer, but there had been a gap in the literature for population-based studies

comparing complication rates in RARC versus open radial cystectomy (ORC). This study aimed to determine the short- and long-term risks of ureter enteric structure by surgical approach (RARC vs. ORC). The SPARED CRN aimed to create a comprehensive clinical database to facilitate patient-centered research for existing and emerging focal therapy technologies.

Party conducting the pilot project and agreement type:

The project was conducted by the MDEpiNet Coordinating Center at the Weill Cornell Medical College, Weill Cornell Medicine-New York Presbyterian Hospital, and the Memorial Sloan Kettering Cancer Center under a cooperative agreement with FDA and support from the Frederick J. and Theresa Dow Wallace Fund of the New York Community Trust.

Specific aim(s):

The project aimed to evaluate differences in the incidence of benign ureter enteric stricture by comparing the stricture rates of RARC and ORC.

Data source(s):

The data source for this project was the Surveillance, Epidemiology, and End Results (SEER)-Medicare data.

Safety outcome(s) of interest:

The safety outcomes of interest were the incidence of benign ureter enteric stricture and the incidence of stricture diagnoses.

Number and names of manufacturers involved:

None.

Number of patients:

There were 1,781 patients who underwent radical cystectomies.

Findings of project:

This project found that RARC was associated with a higher rate of ureter enteric stricture diagnosis and intervention, as the incidence of ureteroenteric stricture at 6 and 12 months was higher for RARC vs. ORC (12.1 percent vs. 7.0 percent and 15.0 percent vs. 9.5 percent, respectively).

Status:

The results of this study were published in *Urology*.[5]

4. Project name: Long-term device outcomes of mesh implants in pelvic organ prolapse (POP) repairs (Women's Health Technology (WHT) CRN)

Description:

The devices involved in this project were mesh implants used in POP repairs. Previous research showed that POP repair with mesh was associated with an increased risk of reoperation when compared with native tissue repair. This project aimed to study the longer-term safety and reintervention outcomes after mesh-based POP repair to inform regulatory and clinical decisions. The purpose of the WHT CRN was to develop tools to facilitate data collection within the existing and new registries and demonstrate that data in the CRN could be used to evaluate the effectiveness and safety of various devices related to women's health.

Party conducting the pilot project and agreement type:

The project was conducted by the MDEpiNet Coordinating Center at the Weill Cornell Medical College, the University of Oxford, and The Warren Alpert Medical School of Brown University under a cooperative agreement with FDA.

Specific aim(s):

This project aimed to assess the long-term reoperation rates following initial POP repair using mesh, compared with those following initial POP native tissue repairs.

Data source(s):

The data source for this project was the New York State Department of Health's Statewide Planning and Research Cooperative System (SPARCS). The study included women undergoing POP repair in inpatient, outpatient, and ambulatory surgical settings in New York State from 2008 to 2016.

Safety outcome(s) of interest:

The safety outcome of interest was the reoperation risk during the follow-up of up to 8 years after the initial POP repair.

Number and names of manufacturers involved:

None.

[5] Alvin C. Goh, Andre Belarmino, Neal A. Patel, Tianyi Sun, Art Sedrakyan, Bernard H. Bochner, Jim C. Hu, A population-based study of ureteroenteric strictures after open and robot-assisted radical cystectomy, Urology (2019).

Number of patients:

The study cohort included 54,194 women undergoing POP repairs (i.e., 12,989 with mesh and 41,205 without mesh) in New York State from 2008 to 2016.

Findings of project:

This project found that POP with mesh was associated with increased long-term risks of reoperation when compared with native tissue repair. The estimated risk of undergoing reintervention at 5 years was 8.8 percent in the mesh group compared with 6.3 percent in the non-mesh group in the matched cohort.

Status:

A manuscript has been submitted for publication in a peer-reviewed journal.

5. Project name: Reoperation and erosion with sling mesh implants for stress urinary incontinence (SUI) (WHT CRN)

Description:

The devices involved in this project were sling mesh implants for SUI. The project aimed to determine the long-term risk of surgical reintervention and erosion after sling implantation and the predictors of these events.

Party conducting the pilot project and agreement type:

The project was led by the MDEpiNet Coordinating Center at the Weill Cornell School of Medicine under a cooperative agreement with FDA.

Specific aim(s):

This project aimed to investigate the long-term risk of reoperation and erosion following SUI sling mesh implantations. The secondary aim was to identify the predictors of long-term reoperation and erosion after SUI sling mesh implantations.

Data source(s):

The New York State Department of Health's SPARCS was used for the data source. The study included women undergoing SUI sling implantations in outpatient and ambulatory surgical settings in New York State from 2008 to 2016.

Safety outcome(s) of interest:

The safety outcomes of interest were the reintervention and occurrence of mesh erosion diagnoses during the follow-up of up to 7 years after the initial SUI repair procedure.

Number and names of manufacturers involved:

None.

Number of patients:

The study cohort included 36,195 women undergoing a sling procedure between 2008 and 2016 in New York State.

Findings of project:

This project found that the estimated risks of a reintervention or erosion diagnosis after sling procedures at 7 years were 6.7 percent and 3.7 percent, respectively. Concomitant pelvic organ prolapse repair and previous hysterectomy were associated with higher risks of reoperation and erosion. The results showed that events continued to accumulate over time and that patients with existing sling mesh devices may benefit from continuous surveillance and evaluations.

Status:

A manuscript has been submitted for publication in a peer-reviewed journal.

VII. Progress on Ongoing Pilot Projects

6. Project name: Electrophysiology Predictable and Sustainable Implementation of National (EP PASSION) Registries - Methods to replace traditional postapproval studies (PASs)

Description:

EP PASSION is an ongoing pilot project that is developing methods to replace traditional mandated PASs with sustainable, reliable, and timely real-world methodology. ICD leads and cardiac re-synchronization therapy (CRT) device leads are involved in this pilot project. Current PASs of high-voltage ICD and CRT leads are conducted in prospective new patient enrollment studies. This current approach is costly, requires years to complete enrollment, and does not always maintain enough patients for follow-up or provide timely answers to postmarket questions. Therefore, this project aims to reduce the cost, duration, and attrition of the PAS through leveraging RWD sources. This pilot is intended to generate more efficient and timely safety and effectiveness data and more quickly identify poorly performing devices.

Party conducting the pilot project and agreement type:

The pilot project is executed by a consortium of voluntary stakeholders including academia, FDA, medical device manufacturers, and professional societies and requires no funding from FDA. The funds for the conduct of the pilot come from the manufacturers involved that are conducting the pilot.

Specific aim(s):

The aims for the five phases of the pilot project are as follows:

- Phase 1 (Complete): Identify the minimal set of core data elements for an assessment of the pacing and defibrillation leads.

- Phase 2 (Ongoing): Determine existing sources of data, which may require formation of several working groups.

- Phase 3 (Ongoing): Develop a method to collect core data elements not available from existing data sources.

- Phase 4 (Ongoing): Develop a linked approach to combine data elements from sources identified or created in Phases 2 and 3.

- Phase 5: Compare the linked data source approach to conventional PAS findings. Peri-procedural and lead/device revision data collection are important for development of the platform for future use in premarket submissions and for devices requiring additional postmarket data to be collected (e.g., leadless pacemakers).

Data source(s):

This pilot project includes administrative claims, device remote monitoring data, manufacturer-device tracking, and complaint handling databases.

Safety outcome(s) of interest:

The safety outcomes of interest include cardiac tamponade, cardiac perforation, and lead adverse events that require surgical intervention such as insulation breach and lead/conductor fracture.

Numbers and names of manufacturers involved:

The four manufacturers involved in the pilot include Abbott, BIOTRONIK, Boston Scientific, and Medtronic.

Number of patients:

The number of patients has not yet been determined.

Findings of project:

The technical work completed to date includes agreement on core minimum data sets, standards for data quality, and methods for linking the registry with outcomes data (such as administrative claims). Validation of the evidence methodologies with the linked data sources, outlined above, is being conducted by manufacturers.

Status:

Ongoing.

7. Project name: Vascular Implants Surveillance Intervention and Outcomes Network (VISION)

Description:

The devices involved in this pilot project are stents, stent-grafts, and other devices used in the treatment of diseases of the peripheral circulatory system. VISION aims to improve evidence generation on the safety and performance of vascular devices and procedures by linking registry data with state and national claims datasets in a distributed data model to monitor the long-term outcomes of patients treated with vascular devices. Linkages between registries and state/national claims datasets may improve follow-up rates and validations of complications, as well as support the risk adjustment of outcomes.

Party conducting the pilot project and agreement type:

The pilot project is being led by the Weill Cornell School of Medicine under a cooperative agreement with FDA. Additional funding is being sought from industry.

Specific aim(s):

The aims of the pilot project are to 1) develop a U.S. national device surveillance network in the vascular device space, 2) bring together registries in a systematic way and obtain longer, more complete patient follow-up information via data linkages, 3) provide a resource for all stakeholders to address the safety and effectiveness of new devices as they enter routine usage, and 4) facilitate and conduct comparative effectiveness studies within a short period after device market entry.

Data source(s):

The data sources for this pilot project include 1) the Society for Vascular Surgery (SVS) Vascular Quality Initiative (VQI) Registry, 2) Medicare claims, 3) the New York State Department of Health's SPARCS, and 4) device manufacturer clinical trial datasets. The pilot project will also include efforts to study the validity of CRN data sources as compared to data

derived from clinical trials.

Safety outcome(s) of interest:

The primary outcomes identified in linked datasets include death, procedure-specific adverse events (stroke, rupture, and amputation), reinterventions, readmissions, surveillance, imaging, and cost.

Numbers and names of manufacturers involved:

Currently, four manufacturers are collaborating on the study: Cook Medical, Endologic, W. L. Gore & Associates, and Medtronic. Additional manufacturers have been approached to participate in this pilot project.

Number of patients:

It is anticipated that data from over 300,000 patients will be used in this pilot project.

Findings of project:

The initial VISION efforts focused on the validation of claims data to capture the outcomes of interest. For example, in one of the studies involving endovascular aortic repair, a medical record review demonstrated a 6 percent 1-year and 16 percent 3-year reintervention rate, and almost all (92 percent) of these events were accurately captured by the linked claims data.[6]

A related study focused on matching registry patients and procedures to their Medicare claims based on an algorithm using indirect identifiers. Such algorithms will help identify and categorize late events after repairs and may serve as a means to enhance the follow-up of patient outcomes.[7]

Building on these efforts, a propensity-matched study was conducted comparing the long-term survival of carotid artery stenting and carotid endarterectomy. In contrast to randomized clinical trial findings, this CRN study demonstrated a survival advantage of stenting over endarterectomy in real-world practice.[8]

Registry-linked datasets have been created for nine procedures. New devices are being added as

[6] Columbo JA, Kang R, Hoel AW, et. al. A Comparison of Reintervention Rates After Endovascular Aneurysm Repair Between the Vascular Quality Initiative Registry, Medicare Claims, and Chart Review. J Vasc Surg. 2019; 69(1):74-76.

[7] Hoel AW, Faerber AE, Moore KO, et. al. A Pilot Study for Long-Term Outcome Assessment After Aortic Aneurysm Repair Using Vascular Quality Initiative Data Matched to Medicare Claims. J Vasc Surg. 2017;66(3):751-759.

[8] Columbo JA, Marinez-Camblor P, MacKenzie TA, et. al. A Comparative Analysis of Long-Term Mortality After Carotid Endarterectomy and Carotid Stenting. J Vasc Surg. 2019;69(1):104-109.

they are approved or cleared for market in the United States.

Status:

The pilot is currently operating and being updated annually.

8. Project name: Ortho CRN (formerly named *ICOR-USA*)

Description:

The Ortho CRN (formerly named *ICOR-USA*) pilot project seeks to apply lessons learned from the International Consortium of Orthopedic Registries to improve clinical evidence generation and safety evaluation for orthopedic implants in the United States via creation of a strategically coordinated registry network.

Party conducting the pilot project and agreement type:

The study is being conducted by the Ortho CRN partners with in-kind support from the various stakeholders.

Specific aim(s):

The aim of this pilot project is to develop surveillance methods to evaluate the safety of arthroplasty devices in the strategically coordinated network of orthopedic registries, called Ortho CRN.

Data source(s):

This pilot project prospectively collected data from the following U.S.-based data sources: KP, the American Joint Replacement Registry (AJRR), the Function and Outcomes Research for Comparative Effectiveness in Total Joint Replacement Registry (FORCE TJR Registry), and the Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI).

Safety outcome(s) of interest:

The primary outcomes of interest for this pilot project are benchmarking performance metrics for hip and knee replacements.

Number and names of manufacturers involved:

Three manufacturers are involved as members of the Steering Committee: Johnson & Johnson, Zimmer Biomet, and Smith & Nephew.

Number of patients involved:

The pilot includes over 1,862,000 total joint replacement procedures.

Findings of project:

Pending.

Status:

Ongoing.

Of note: NESTcc awarded additional funding for the development of Objective Performance Criteria, which will be reported in the update next year.

VIII. Pilot Projects Initiated in 2019

9. Project name: VQI-DELTA Paclitaxel (PTX) study

Description:

In 2018, a published meta-analysis identified an association between the use of PTX drug coated balloons (DCBs) or drug-eluting stents (DESs) used to treat peripheral arterial disease (PAD) with increased mortality at 2 and 5 years after treatment, when compared to patients treated with non-PTX-coated or eluting devices.[9] Consequently, FDA has issued safety communications,[10, 11, 12] initiated additional review of the mortality signal, and convened an advisory panel.[13]

Party conducting the pilot project and agreement type:

The pilot project is being led by the Leahy Clinic under a cooperative agreement with FDA in communication with the MDEpiNet Registry Assessment of Peripheral Devices effort, a private-public partnership of academia, industry, and governmental regulatory agencies dedicated to improving the national evaluation of peripheral arterial devices throughout these devices' total

[9] Katsanos,K, Spiliopoulos,S , Kitrou, P, Krokidis, M, Karnabatidis,D. Risk of Death Following Application of Paclitaxel-Coated Balloons and Stents in the Femoropopliteal Artery of the Leg: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Am Heart Assoc. 2018; 7(24):e011245.

[10] See https://www.fda.gov/medical-devices/letters-health-care-providers/treatment-peripheral-arterial-disease-paclitaxel-coated-balloons-and-paclitaxel-eluting-stents.

[11] See https://www.fda.gov/medical-devices/letters-health-care-providers/update-treatment-peripheral-arterial-disease-paclitaxel-coated-balloons-and-paclitaxel-eluting.

[12] See https://www.fda.gov/medical-devices/letters-health-care-providers/august-7-2019-update-treatment-peripheral-arterial-disease-paclitaxel-coated-balloons-and-paclitaxel.

[13] See https://www.fda.gov/advisory-committees/advisory-committee-calendar/june-19-20-2019-circulatory-system-devices-panel-medical-devices-advisory-committee-meeting.

product lifecycle.

Specific aim(s):

This study seeks to assess the comparative safety of PTX DCBs and DESs in the treatment of PAD through analysis of the VQI Peripheral Vascular Intervention (PVI) registry module using the DELTA system.

This project will evaluate the relative safety of PTX used as an antiproliferative agent in the treatment of symptomatic PAD, analyzing PTX DCB and PTX DES, both together and as unique exposures, using propensity score-matched survival analysis. The VQI PVI dataset will be used to maximize the consistency of outcome and clinical covariate definitions.

Data sources(s):

This study will leverage clinical data regarding the treatment of PAD through the VQI data collected by the Society of Vascular Surgeons (SVS). Since 2004, the SVS has collected detailed clinical data regarding the treatment of PAD through the VQI in over 550 hospitals in North America and contains data on over 575,000 patients. The VQI has begun linkage with the Global Unique Device Identification Database to identify devices and linkage with the Social Security Death Index to ascertain vital status over time.

The DELTA surveillance system was developed to assess potential medical device safety concerns. DELTA has been previously validated for prospective monitoring of clinical registries and clinical datasets and is available as an open source software tool with associated technical documentation.

Safety outcome(s) of interest:

The primary safety outcome of interest is survival (i.e., freedom from death from any cause) at 2 years post intervention in three cohorts of patients: 1) patients treated with PTX-DCB, 2) patients treated with PTX-DES, and 3) patients treated with either PTX DCB or DES analyzed together.

Numbers and names of manufacturers involved:

Five manufacturers are involved: Bard, Medtronic, Philips, Cook, and Boston Scientific.

Number of patients:

Anticipate a total sample of 5,700 PTX-DES- and 25,200 PTX-DCB-treated patients would be captured, with 1,865 PTX-DES and 8,250 PTX-DCB patients having been followed for a minimum of 2 years.

Findings of project:

Initial results should be available for FDA's next annual report.

Status:

Ongoing.

10. Project name: Creating a national surveillance infrastructure for devices used in hernia repairs

Description:

The Abdominal Core Health CRN aims to address the long-term surveillance of techniques and devices commonly used in the care of abdominal core health. As part of this effort, the CRN aims to improve data infrastructure through linkage of registry data with administrative and clinical data, which may improve longitudinal and cross-facility follow-up rates as well as validation of complications and devices.

Party conducting the pilot project and agreement type:

The pilot project is being led by the Weill Cornell Medical College under a cooperative agreement with FDA. Cornell has also contracted with the Americas Hernia Society Quality Collaborative (AHSQC).

Specific aim(s):

The primary aims of this pilot study were to link registry and state claims data to 1) examine data completeness and to determine the feasibility of an effective linkage model in the abdominal core health space (successfully executed), 2) assess long-term follow-up rates, and 3) determine long-term catastrophic complications following ventral hernia repair.

Data source(s):

The data sources for this pilot project include 1) the New York State Department of Health's SPARCS claims data and 2) the AHSQC hernia patient registry data.

Safety outcome(s) of interest:

The primary outcomes to be identified in linked datasets include hernia recurrence, readmission, re-operation, surgical site infection, and mesh-related complications.

Numbers and names of manufacturers involved:

None.

Number of patients involved:

There were 737 registry patients that were identified in the AHSQC registry who had undergone hernia repair in New York State from 2015 to 2016.

Findings of project:

A total of 737 New York State patients were identified from the AHSQC registry for linkage. SPARCS data were available through 2016, and therefore, 577 registry patients whose date of repair occurred in 2017 or later were excluded. Of the remaining 160 registry patients qualified for linkage, 88.1 percent (N=141) were successfully linked to SPARCS claims data using a sequential matching algorithm. The long-term outcomes are being analyzed to determine follow-up and complication rates.

Status:

Ongoing.

IX. Conclusion

A variety of active surveillance pilot projects are currently underway, several of which are already producing RWE for device evaluation by various stakeholders, including FDA and industry. In addition, the voluntary pilot projects will help inform the development of active surveillance and practical applications of active surveillance in real-world settings. These efforts are important to the further development of NEST and other RWE capabilities, and the future work outlined here will increase the scale and impact of these capabilities.

Appendix: Summary Table of Device Pilot Projects Under Section 708 of FDARA

#	Pilot name	Device(s) Involved	Data Source(s) Involved	Safety Outcome(s) of Interest	Manufacturers Involved	Status	# of Patients	Agreement Type
1	Signal detection: Opioid use and risk of joint revision surgery	Total knee and total hip	KP's TJR Registry and EHRs	Risk of revision surgery	Johnson & Johnson, Smith & Nephew, Zimmer Biomet	Completed	24,105 (knees) 12,895 (hips)	Cooperative agreement with FDA
2	DELTA-ICD leads	ICD leads	ICD Registry in the NCDR	Survival (freedom from failure)	No formal involvement yet, but plan to include industry on the steering committee	Completed	374,132	Cooperative agreement with FDA and funding from the William M. Wood Found.
3	SPARED robot-assisted cystectomy	Robotic devices	SEER-Medicare data	Benign ureter stricture and stricture diagnoses	None	Completed	1,781 patients	Cooperative agreement with FDA
4	WHT-CRN mesh for POP repairs	Mesh implants used in POP repairs	SPARCS	Reoperation risk	None	Completed	54,194 patients	Cooperative agreement with FDA
5	WHT-CRN slight mesh for SUI	Sling mesh implants for SUI	SPARCS	Reoperation and erosion	None	Completed	36,195 patients	Cooperative agreement with FDA

#	Pilot name	Device(s) Involved	Data Source(s) Involved	Safety Outcome(s) of Interest	Manufacturers Involved	Status	# of Patients	Agreement Type
6	EP PASSION	IICD leads and cardiac re-synchronization therapy device leads	Administrative claims, device remote monitoring data, manufacturer-device tracking, and complaint handling databases	Cardiac tamponade and perforation, lead adverse events that require surgical intervention	Abbott, BIOTRONIK, Boston Scientific, Medtronic	Ongoing	Not yet determined	No funding for phase 1, but funding from industry for subsequent phases
7	VISION	Stents, stent-grafts, and other devices used in the treatment of diseases of the peripheral circulatory system	SVS VQI Registry, Medicare claims, SPARCS, device manufacturer clinical trial databases	Death, procedure-specific adverse events (stroke, rupture, and amputation), reinterventions, readmissions, surveillance, imaging, cost	Cook Medical, Endologic, Gore & Assoc., Medtronic	Ongoing	Anticipate 300,000 patients	Cooperative agreement with FDA; seeking funding from industry for next phase
8	Ortho CRN (formerly named *ICOR-USA*)	Joint replacements	Ortho CRN members: KP, AJRR, FORCE TJR, and MARCQI	Revision rates	Zimmer Biomet, Smith & Nephew, Johnson & Johnson	Ongoing	>1,862,000 patients	Cooperative Agreement with FDA
9	VQI-DELTA PTX study	PTX DCBs and PTX DESs	VQI data collected by SVS	Survival (i.e., freedom of death from any cause)	Medtronic, Bard, Philips, Cook, and Boston Scientific	Ongoing	5,700 PTX-DES and 25,200 PTX-DCB patients	Cooperative Agreement with FDA

#	Pilot name	Device(s) Involved	Data Source(s) Involved	Safety Outcome(s) of Interest	Manufacturers Involved	Status	# of Patients	Agreement Type
10	Creating a national surveillance infrastructure for devices used in hernia repairs	Mesh for ventral hernia repair	SPARCS and AHSQC	Hernia recurrence, readmission, re-operation, surgical site infection, and mesh-related complications	None	Ongoing	737 registry patients	Cooperative agreement with FDA
Terminated/Discontinued Studies								
	DELTA-TAVR	Aortic and mitral valves	NCDR's Transcatheter Valve Therapy Registry	Survival (i.e., freedom from a composite of death, stroke, or repeat valve operations)	Medtronic, Abbott, Edwards	Discontinued	> 150,000 patients	Cooperative agreement with FDA
	WHT-CRN Urogynecological Mesh and Risk of Cancer	Mesh	SPARCS	Cancer	None	Discontinued	59,117 patients	Cooperative agreement with FDA