Report to Congress

Device Pilot Projects

FY 2021

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

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). Section 708 of 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; this report must contain a description of the pilot projects being conducted and the pilot projects being continued or expanded pursuant to that section. This is the fourth annual report by the U.S. 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 for medical devices. For the pilot projects, *active surveillance* refers to actively and continuously generating information on the device's performance and on the clinical outcomes associated with the use of the device in routine clinical practice. Active surveillance of medical devices may be understood relative to FDA's traditional or "passive surveillance," which is an approach that relies on users notifying FDA of device-related events (e.g., through adverse event reporting). 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 an 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.

In general, 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 the device's safety, including adverse events, malfunctions, and other safety information. This information is presented in the report and summarized in the Appendix.

This report features nine device pilot studies, including seven that have been completed and two

that are ongoing. Of note, five of the nine reported studies were initiated in fiscal year (FY) 2021 (October 1, 2020, to September 30, 2021), and all five new studies were also completed in the same fiscal year. The pilot projects detailed in this report are at various stages of development and include several device types. This report includes two groups of projects: (1) pilot projects completed in FY 2021 and (2) pilot projects that were ongoing as of October 2021 (which is part of FY 2022, running from October 1, 2021, to September 30, 2022). The data sources leveraged in the presented pilot projects are both national- and state-based, and they include EHRs, registries, and claims. The devices studied include orthopedic joint implants, implantable cardioverter defibrillators, vascular implants, prostate ablation devices, and ventral hernia mesh devices. A cumulative summary of all completed projects from previous reports is included in the Appendix.

Several of these pilot projects are already producing RWE for device evaluation by various stakeholders, including FDA and industry. These projects have helped and will continue to inform the development and practical applications of active surveillance in real-world settings. These efforts are important to the further development of the 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

AAA	Abdominal Aortic Aneurysm
ACHQC	Abdominal Core Health Quality Collaborative
BPH	Benign Prostrate Hyperplasia
CRN	Coordinated Registry Network
CRT	Cardiac Re-Synchronization Therapy
DELTA	Data Extraction and Longitudinal Trend Analysis
EHR	Electronic Health Record
EP PASSION	Electrophysiology Predictable and Sustainable Implementation of National Registries
EVAR	Endovascular Aneurysm Repair
FDA	U.S. Food and Drug Administration
FDARA	FDA Reauthorization Act of 2017
FY	Fiscal Year
HIVE	High-Performance Integrated Virtual Environment
ICD	Implantable Cardioverter Defibrillator
MDEpiNet	Medical Device Epidemiology Network
MIST	Minimally Invasive Surgical Therapies
NEST	National Evaluation System for health Technology
NESTcc	National Evaluation System for health Technology Coordinating Center
NLP	Natural Language Processing
OSHPD	Office of Statewide Health Planning and Development
PAS	Postapproval Study
PTX	Paclitaxel
PUL	Prostatic Urethral Lift
RWD	Real-World Data

RWE	Real-World Evidence
SPARCS	Statewide Planning and Research Cooperative System
SPARED	Study of Prostate Ablation-Related Energy Devices
SVS	Society of Vascular Surgeons
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). Section 708 of 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 that contains a description of the pilot projects being conducted and the pilot projects being continued or expanded pursuant to that section.

II. Background on Section 708

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

Some of the ways in which FDA has used active surveillance strategies for monitoring medical device safety include the following:

- Conducting ongoing systematic monitoring of an existing high-quality granular data source with a system that provided regular feedback regarding safety alerts 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 effectiveness and durability of them.

- Using a pre-defined algorithm to detect potential safety signals 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 collaborators and is primarily involved in advancing the strategically Coordinated Registry Networks (CRNs) featured in the pilot studies.

As intended by the law, this report has been prepared to contribute to an independent third-party's evaluation of the strengths, limitations, and appropriate uses of evidence collected pursuant to the 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.

In general, the Center for Devices and Radiological Health at FDA has documented an increase in the use of RWE to support regulatory decision-making, as documented by a report released in March 2021 featuring 90 publicly available examples of different types of regulatory submissions supported by RWE.[1] 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. Therefore, the pilot projects involve devices and device types for which the collection and analysis of RWE regarding the devices' safety and effectiveness is likely to advance public health.

The pilot projects reported here are at various stages of development and include several device types. The data sources are both national- and state-based, and they include EHRs, registries, and claims. The devices studied include orthopedic joint implants, implantable cardioverter

[1] *See* Examples of Real-World Evidence (RWE) Used in Medical Device Regulatory Decisions: Selected examples with file summaries, details on real-world data source, populations, and descriptions of use by the Center for Devices and Radiological Health, available at https://www.fda.gov/media/146258/download; *see also* the accompanying FDA Voices document titled Leveraging Real World Evidence in Regulatory Submissions of Medical Devices, originally posted on March 16, 2021, available at https://www.fda.gov/news-events/fda-voices/leveraging-real-world-evidence-regulatory-submissions-medical-devices.

defibrillators (ICDs), vascular implants, prostate ablation devices, and ventral hernia mesh devices.

Several of these projects have produced RWE for device evaluation (premarket and postmarket) by various stakeholders, including FDA and industry. In addition, these projects provide FDA and industry with 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 ongoing work outlined here will increase the scale and impact of these capabilities.

All pilot projects comply with the law's requirements to have established security measures to maintain confidentiality and privacy of certain data.

The persons or organizations conducting these pilot projects have high levels of research, statistical, epidemiologic, data science, informatics, and/or clinical capability and expertise to conduct and complete the activities. As applicable, pilot projects are conducted under contracts, cooperative agreements, grants, or other appropriate agreements 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's name
- Description of the project and devices involved
- Party conducting the pilot project
- Agreement type (e.g., contract, cooperative agreement, grant)
- Specific aim(s) of the project
- Data source(s) involved
- Safety outcome(s) of interest
- Numbers and names of manufacturers involved
- Number of patients
- Findings of the project
- Status (as of October 2021)

The manufacturer's involvement in a project is defined broadly for this report. For example, 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. The Appendix also includes the cumulative list of all the projects previously reported.

Nine studies were conducted in FY 2021. Specifically, the following five studies were initiated and completed in FY 2021:

1. Examining Outcomes After Benign Prostatic Hyperplasia Minimally Invasive Surgical Procedures Using State All-Payer Databases

2. Long-Term Evaluation of Type II Endoleak Using Vascular Quality Initiative and Linked Medicare Claims

3. Association Between Device Type and Long-Term Risks of Reintervention and Late Abdominal Aortic Aneurysm Rupture Among Patients Treated with Endovascular Aneurysm Repair

4. Two-Year Revision Rates in Total Ankle Replacements Versus Ankle Arthrodesis – A Population-Based Propensity Score-Matched Comparison from New York and California

5. Mortality After Paclitaxel-Coated Balloon Angioplasty and Stenting of Superficial Femoral and Popliteal Artery in the Vascular Quality Initiative

In addition, two of the nine studies were reported as ongoing in the FY 2020 Annual Report and were completed in FY 2021.

The status of these seven studies is captured in sections V and VI of this report, along with the two remaining pilot projects that, in FY 2021, were still ongoing from the previous fiscal years. Specifically, section V presents the findings from the seven pilot projects completed in FY 2021 (which include the five that were initiated and completed in FY 2021 and the two that had been ongoing in the FY 2020 report but were completed in FY 2021). Section VI provides updates for two pilot projects that are still ongoing from FY 2020.

A note about CRNs, which are frequently mentioned in this report: typically, CRNs are partnered, registry-based RWD sources that include registry data linked to other sources, such as claims, EHRs, and patient-generated data to enable studies of long-term outcomes via longitudinal patient healthcare profiles.

V. Completed Pilot Projects

The findings from the seven pilot projects completed in FY 2021 are presented below.

1. Project Name: Examining Outcomes After Benign Prostatic Hyperplasia Minimally Invasive Surgical Procedures Using State All-Payer Databases

a. Description and devices involved

Benign prostatic hyperplasia (BPH) is a common condition causing lower urinary tract symptoms in aging men. Trans Urethral Resection of the Prostate is a standard surgical treatment of BPH.

Recently, minimally invasive surgical procedures like Prostatic Urethral Lift (PUL), Trans Urethral Needle Ablation, and Trans Urethral Microwave Therapy that use medical devices have emerged for the relief of urinary symptoms and the reduction of surgical morbidity and length of hospital stay. The PUL is a surgical procedure that uses a permanent implant; Trans Uretrhal Needle Ablation uses radiofrequency needles; and Trans Urethral Microwave Therapy uses an instrument that emits microwave energy. There is a need to assess the surgical effectiveness or reproducibility of these procedures in a real-world population using a large dataset.

b. Party conducting the pilot project

The MDEpiNet Coordinating Center at Weill Cornell Medicine.

c. Agreement type (e.g., contract, cooperative agreement, grant)

Cooperative agreement with FDA.

d. Specific aim(s)

To investigate the differences in surgical outcomes between PUL and other minimally invasive surgical proceduress.

e. Data source(s) involved

Data from the New York State Department of Health's Statewide Planning and Research Cooperative System (SPARCS) and the California Office of Statewide Health Planning and Development (OSHPD).

f. Safety outcome(s) of interest

The short-term outcomes of interest in this pilot project included rates of hospital readmission due to acute urinary retention, hematuria, and urinary tract infection at 30 and 90 days following

the index BPH surgery. Risk of reoperation and developing urethral stricture were evaluated at 1 year, 3 years, and 5 years following the index BPH surgery.

g. Numbers and names of manufacturers involved

None.

h. Number of patients

A total of 2,694 patients participated in this study.

i. Findings of project

PUL patients had lower 30 day and 90-day hospital readmissions compared to those undergoing other minimally invasive surgical procedures. PUL patients also had lower readmissions related to urinary retentions .

j. Status

Completed. A manuscript of this study is in progress.

2. Project Name: Long-Term Evaluation of Type II Endoleak Using Vascular Quality Initiative and Linked Medicare Claims

a. Description and devices involved

Endovascular aneurysm repair (EVAR) using endovascular grafts is associated with lower short-term morbidity and mortality than open surgical repair, but there are gaps in clinical evidence regarding the long-term outcomes associated with the procedure. Prior studies evaluating the significance of type II endoleaks after EVAR using retrospective single center datasets, prospective post-market registries, and insurance claims showed a high incidence of type II endoleaks. However, these studies have limitations in terms of the size of their patient cohorts and the length and duration of outcomes. The study aimed to evaluate the natural history and significance of type II endoleaks using data from the Society for Vascular Surgery (SVS) – Vascular Quality Initiative (VQI) linked to Medicare claims (VQI-Medicare) via the Vascular Implant Surveillance and Interventional Outcomes Network (VISION) database.

b. Party conducting the pilot project

The MDEpiNet Coordinating Center at Weill Cornell.

c. Agreement type (e.g., contract, cooperative agreement, grant)

Cooperative agreement with FDA.

d. Specific aim(s)

To evaluate the natural history and significance of type II endoleaks using data from SVS – VQI-Medicare via the VISION database.

e. Data source(s) involved

SVS VQI-Medicare

f. Safety outcome(s) of interest

The main outcomes of interest in this pilot project included rates of mortality, rates of reintervention, rates of type II endoleak-specific reinterventions, and the frequency of follow-up imaging at 1 and 2 years.

g. Numbers and names of manufacturers involved

None.

h. Number of patients

A total of 6,079 patients participated in this study.

i. Findings of project

There was no difference in survival and reintervention rates between (1) patients who had a type II endoleak within 1 and 2 years after the EVAR procedure and (2) those who did not.

j. Status

Completed. A manuscript of this study is in progress.

3. Project Name: Association Between Device Used and Long-Term Risks of Reintervention and Late Abdominal Aortic Aneurysm Rupture Among Patients Treated with Endovascular Aneurysm Repair

a. Description and devices involved

Four endovascular graft devices (Cook Zenith, Endologix AFX, Gore Excluder, and Medtronic Endurant) are commonly used in the United States for EVAR of abdominal aortic aneurysm (AAA). One of the four devices, the Endologix AFX device, was modified in 2015 after reports that fabric leaks were associated with higher risks of long-term reintervention or late AAA rupture.[2] This pilot aimed to determine if reintervention or late AAA rupture was associated with the device types used for this procedure.

[2] *See* FDA's Safety Communication on the use of Endologix AFX Endovascular AAA Graft System, available at https://www.fda.gov/medical-devices/safety-communications/update-fda-reminds-patients-and-health-care-providers-importance-least-yearly-lifelong-follow-use.

b. Party conducting the pilot project

The MDEpiNet Coordinating Center at Weill Cornell Medicine.

c. Agreement type (e.g., contract, cooperative agreement, grant)

Cooperative agreement with FDA.

d. Specific aim(s)

To (1) determine the long-term rate of reintervention and AAA rupture after EVAR, including with the Endologix AFX device (3 years post procedure) and other available devices (at least 5 years post procedure), in a national setting; (2) study if the 2015 change in the Endologix AFX device was associated with a change in reintervention or late rupture relative to other concomitantly utilized devices (such as multiple stents in different anatomic locations); and, (3) study the association between the device used, reintervention, and AAA rupture using clinical data from VQI-Medicare via the VISION database.

e. Data source(s) involved

VQI-Medicare datavia the VISION database.

f. Safety outcome(s) of interest:

The safety outcomes of interest in this pilot project included the reintervention rates and AAA rupture rates after EVAR.

g. Numbers and names of manufacturers involved

None.

h. Number of patients

A total of 21,213 patients participated in this study.

i. Findings of project

Long-term EVAR outcomes varied by device, suggesting the need for long-term device-specific surveillance and reporting.

j. Status

Complete. A manuscript of this study is in progress.

4. Project Name: Two-Year Revision Rates in Total Ankle Replacements Versus Ankle Arthrodesis – A Population-Based Propensity Score-

Matched Comparison from New York and California

a. Description and devices involved

Ankle arthrodesis is the established surgical treatment for end-stage ankle arthritis, but total ankle replacement is increasing. Few studies have compared clinical outcomes between primary total ankle replacement and ankle arthrodesis in real-world use. The pilot aimed to compare outcomes following ankle arthrodesis and total ankle replacement when they were used as a surgical treatment of end-stage ankle arthritis.

b. Party conducting the pilot project

The MDEpiNet Coordinating Center at Weill Cornell Medicine.

c. Agreement type (e.g., contract, cooperative agreement, grant)

A cooperative agreement with FDA.

d. Specific aim(s)

To investigate 2-year revision rates after total ankle replacement and ankle arthrodesis procedures in New York and California.

e. Data source(s) involved

Longitudinal data from the New York State Department of Health's SPARCS from October 2015 to December 2018 and the California OSHPD from October 2015 to December 2017.

f. Safety outcome(s) of interest

The primary outcome of interest for this pilot project included revision after the primary total ankle replacement and ankle arthrodesis procedures. Secondary outcomes were in-hospital complications and below-knee amputations. Propensity score-matching adjusted for differences in baseline characteristics. To determine predictors of the main outcome, each group was analyzed separately using multivariable Cox regressions.

g. Numbers and names of manufacturers involved

None.

h. Number of patients

A total of 1,477 total ankle replacementand 1,468 ankle arthrodesis patients participated in this study.

i. Findings of project

There was no difference in long-term revision after total ankle replacement and ankle arthrodesis. Among total ankle replacement patients, older individuals had fewer revisions, and among ankle arthrodesis patients, females had fewer revisions.

j. Status

Completed. A manuscript of this study is in progress.

5. Project Name: Changes in the Long-Term Risk of Adverse Outcomes in Patients Treated with Open and Endovascular Abdominal Aortic Aneurysm Repairs

a. Description and devices involved

EVAR has been widely adopted in the past 20 years. Recent publications note that the early benefits of EVAR were lost after 6-36 months, trending towards the imposition of long-term harms. This pilot project aimed to assess long-term outcomes following EVAR using endovascular grafts.

b. Party conducting the pilot project

The MDEpiNet Coordinating Center at Weill Cornell Medicine.

c. Agreement type (e.g., contract, cooperative agreement, grant)

A cooperative agreement with FDA.

d. Specific aim(s)

To compare mortality and reintervention rates after index repair for EVAR and open aneurysm repair procedures performed before and after January 2010.

e. Data source(s) involved

The VQI-Medicare data- via the VISION database.

f. Safety outcome(s) of interest

The safety outcomes of interest for this pilot project included the mortality and reinterventions after index repair for procedures performed before and after January 2010.

g. Numbers and names of manufacturers involved

None.

h. Number of patients

A total of 246,333 EVAR and 124,559 open aneurysm repair patients participated in this study.

i. Findings of project

Patients undergoing EVAR had higher mortality and reintervention rates than those undergoing open aneurysm repair. When comparing mortality and reintervention rates for each type of procedure performed before and after 2010, there has been no difference in mortality rates for either procedure and a small difference in reintervention rates with each procedure.

j. Status

Completed. A manuscript of this study is in progress.

6. Project Name: Electrophysiology Predictable and Sustainable Implementation of National (EP PASSION) Registries - Methods to Replace Traditional Postapproval Studies (PASs)

a. Description

EP PASSION is a pilot project that developed methods to replace traditional, mandated PASs with sustainable, reliable, and timely real-world methodology. ICD leads and cardiac re-synchronization therapy device leads were involved in this pilot project. Current PASs of high-voltage ICD and cardiac resynchronization therapy 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 aimed to reduce the cost, duration, and attrition of the PAS through leveraging RWD sources. This pilot was intended to generate more efficient and timely safety and effectiveness data and more quickly identify poorly performing devices.

b. Party conducting the pilot project

The pilot project was executed by a consortium of voluntary stakeholders, including academia, FDA, medical device manufacturers, and professional societies. This project required no funding from FDA; instead, the funds for the conduct of the pilot came from the manufacturers involved in the pilot.

c. Agreement type (e.g., contract, cooperative agreement, grant)

None.

d. Specific aim(s)

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

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

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

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

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

- Phase 5 (Completed): Compare the linked data source approach to conventional PAS findings.

e. Data source(s)

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

f. Safety outcome(s) of interest

The safety outcomes of interest in this pilot project included cardiac tamponade, cardiac perforation, and lead adverse events that required surgical intervention (such as an insulation breach or lead/conductor fracture).

g. Numbers and names of manufacturers involved

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

h. Number of patients

A total of 64,977 patients from six PASs participated in this study.

i. Findings of project

The technical work completed included an agreement on core minimum data sets, standards for data quality, and methods for linking device registration and complaint data with outcomes data (such as administrative claims). Seven validation studies were conducted across four manufacturers, encompassing 64,977 patients across six PASs. There was consistency in the ability to capture specific outcomes, such as complication rates for lead adverse events (e.g., fracture) between traditional follow-up and EP PASSION post-approval methodologies in the majority of the validation studies.

j. Status

Completed. A manuscript of this study is in progress.

7. Project Name: Mortality After Paclitaxel-Coated Balloon Angioplasty and Stenting of Superficial Femoral and Popliteal Artery

a. Description and devices involved

The MDEpiNet's VISION CRN uses RWD for tracking outcomes, such as late mortality, after use of paclitaxel (PTX)-coated or eluting devices (i.e., balloons and stents) to treat peripheral artery disease. This project involved a large, observational, registry linked with Medicare data to study PTX-related mortality in the treatment of peripheral artery disease to inform the development of methods and systems for active surveillance.

b. Party conducting the pilot project

The MDEpiNet Coordinating Center at Weill Cornell Medicine.

c. Agreement type (e.g., contract, cooperative agreement, grant)

A cooperative agreement with FDA.

d. Specific aim(s)

To compare mortality rates after treatment of superficial femoral-popliteal artery disease with PTX devices and non-PTX devices using a multicenter vascular registry.

e. Data source(s)

The data sources for this pilot project included the VISION CRN, which consists of the VQI-Medicare data for a long-term surveillance evaluation.

f. Safety outcome(s) of interest

The outcome of interest for this pilot project included the mortality rate after treatment of superficial femoral-popliteal artery disease with PTX devices and non-PTX devices.

g. Numbers and names of manufacturers involved

Most manufacturers of PTX devices and non-PTX devices for treating peripheral artery disease were involved.

h. Number of patients involved

A total of 11,452 patients that underwent endovascular treatment of superficial femoral-popliteal

artery disease from October 2016 to December 2019 were identified in the SVS VQI database and included in this pilot project. Linkage with Medicare data was completed.

i. Findings of project

In this cohort study, PTX-coated devices used in the treatment of occlusive disease were not associated with increased mortality. This finding was consistent across three cohorts of patients: (1) those with femoropopliteal and infrapopliteal disease with or without concurrent treatment of other lower extremity arteries, (2) those with isolated superficial-femoral or popliteal artery disease, and (3) those with characteristics that approximated randomized controlled trials populations.

j. Status

Completed. A manuscript of this study is in progress.

VI. Progress on Ongoing Pilot Projects

The findings from the two ongoing pilot projects are presented below.

8. Project Name: Creating a National Surveillance Infrastructure for Devices Used in Hernia Repairs

a. Description and devices involved

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

b. Party conducting the pilot project

The MDEpiNet Coordinating Center at Weill Cornell Medicine.

c. Agreement type (e.g., contract, cooperative agreement, grant)

A cooperative agreement with FDA.

d. Specific aim(s)

The primary aims of this pilot study are 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.

e. 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 Abdominal Core Health Quality Collaborative (ACHQC) hernia patient registry data.

f. Safety outcome(s) of interest

The primary outcomes to be identified in linked datasets include hernia recurrences, hospital readmissions, reoperations, surgical site infections, and mesh-related complications.

g. Numbers and names of manufacturers involved

None.

h. Number of patients involved

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

i. Findings of project

A total of 737 New York State patients were originally identified from the ACHQC 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% (N=141) were successfully linked to SPARCS claims data using a sequential matching algorithm. An analysis of additional SPARCS data for 2017 and 2018 is ongoing to support the project's aims of assessing long-term outcomes and determining follow-up and complication rates. Next steps in this project include identifying patients eligible for linkage in the ACHQC registry and then performing that linkage.

j. Status

Ongoing.

9. Project Name: Active Surveillance of Medical Device Safety and Outcomes Using EHRs: Prostate Cancer Partial Gland Ablation Technologies

a. Description and devices involved

The primary objective of this project is to develop Natural Language Processing (NLP) methodologies using EHR data to perform an active surveillance of medical device safety and

outcomes for prostate cancer therapies, including partial gland ablation. The project also aims to integrate the data into the Study of Prostate Ablation-Related Energy Devices (SPARED) CRN registry with the help of High-Performance Integrated Virtual Environment (HIVE) technologies at the MDEpiNet Coordinating Center at Weill Cornell Medicine.

b. Party conducting the pilot project

The MDEpiNet Coordinating Center at Weill Cornell Medicine.

c. Agreement type (e.g., contract, cooperative agreement, grant)

A cooperative agreement with FDA.

d. Specific aim(s)

The specific aims of this project are as follows: (1) collect data from EHRs with manual data extraction of cancer characteristics from pathology and radiology reports, (2) develop and validate NLP tools by developing sustainable and scalable strategies to supplement the existing NLP infrastructure to support active surveillance of partial gland ablation, and (3) develop and add active surveillance statistical methodology to the data ecosystem.

e. Data source(s)

The data sources for this project include the EHRs at Weill Cornell Medicine.

f. Safety outcome(s) of interest

The specific outcomes of interest are the data elements harvested from EHRs into the NLP and HIVE repository that are integrated into the SPARED registry.

g. Numbers and names of manufacturers involved

None.

h. Number of patients involved

A total of 111 patients participated.

i. Findings of project

During the first phase, NLP algorithms were utilized to conduct EHR queries and to extract findings from biomedical reports. Magnetic resonance imaging reports and biopsy reports were processed to extract structured findings. During the second phase, the performance of the NLP was assessed in 111 MRI and biopsy reports by comparing NLP outputs to the gold standard, manually reviewed and labeled MRI reports. The performance of NLP was assessed on the entity level. A total of 524 entities were compared between NLP output and manually labeled MRI reports. Overall, Positive Predictive Value was over 99% after two rounds of NLP process

improvements. The NLP is considered adequate and reasonable for real-world studies, and it was implemented in HIVE. The third phase of the study is underway.

j. Status

Ongoing.

VII. Conclusion

A variety of active surveillance pilot projects are already producing RWE for device evaluation by various stakeholders, including FDA and industry. In addition, the voluntary pilot projects have and will continue to 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 the 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 the FDA Reauthorization Act of 2017

#	Pilot Name	Device(s) Involved	Data Source(s) Involved	Safety Outcome(s) of Interest	Manufacturers Involved	Status	# of Patients	Agreement Type
Pilot Projects for Current Reporting Period								
1.	Examining Outcomes After Benign Prostatic Hyperplasia Minimally Invasive Surgical Procedures Using State All Payer Databases,	Prostatic urethral lift, Trans Urethral Needle Ablation, and Trans Urethral Microwave Therapy, Devices (permanent implants, radiofrequency needles, and microwave-emitting devices)	Data from the New York State Department of Health's Statewide Planning and Research Cooperative System (SPARCS) and the California Office of Statewide Health Planning and Development (OSHPD)	Rates of hospital readmission due to acute urinary retention, hematuria, and urinary tract infection at 30 and 90 day following the index BPH surgery. Risk of reoperation and developing urethral stricture at 1, 3, and 5 years following the index BPH surgery.	None	Completed	2,694	A cooperative agreement with the U.S. Food and Drug Administration (FDA).
2	Long Term Evaluation of Type II Endoleak Using Vascular Quality Initiative and Linked	Endovascular grafts	VQI,Medicare claims data viaVascular Implants Surveillance Intervention	Mortality, reintervention, type II endoleak specific reintervention, and frequency	None	Completed	6,079	A 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
	Medicare Claims		and Outcomes Network (VISION)	of follow-up imaging at 1 and 2 years				
3	Association Between Devices and Long-Term Risks of Reintervention and Late Abdominal Aortic Aneurysm Rupture Among Patients Treated with Endovascular Aneurysm Repair	Endovascular grafts	VQI - Medicare datavia VISION database	Reintervention and abdominal aortic aneurysm rupture after endovascular aneurysm repair (EVAR)	None	Completed	21,213 patients	A cooperative agreement with FDA.
4	Two-Year Revision Rates in Total Ankle Replacements Versus Ankle Arthrodesis – A Population-Based Propensity Score-Matched Comparison from New York and California	Ankle arthrodesis and total ankle replacement devices	Data from New York SPARCS and the California OSHPD	Revision after the index total ankle replacement and ankle arthrodesis procedures, in-hospital complications and below-knee amputations	None	Completed	1,477 total ankle replacements and 1,468 ankle arthrodesis	A cooperative agreement with FDA.
5	Changes in the Long-Term Risk of Adverse Outcomes in	Endovascular grafts	The VQI-Medicaldata via VISION	Long-term mortality (at least 3 years) and	None	Completed	246,333 EVAR and 124,559 open aneurysm repair	A 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
	Patients Treated with Open and Endovascular Abdominal Aortic Aneurysm Repairs			reintervention				
6	Electrophysiology Predictable and Sustainable Implementation of National Registries (EP PASSION)	Implantable Cardioverter Defibrillator (ICD) 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, and Medtronic	Completed	64,777 patients	None
7	Mortality After Paclitaxel Coated Balloon Angioplasty and Stenting of Superficial Femoral and Popliteal Artery in the Vascular Quality Initiative	Paclitaxel (PTX) balloons and stents and non-PTX balloons and stents	VQI-Medicare data via VISION	Mortality	Most manufacturers of PTX devices and non-PTX devices	Completed	11,452 patients	A cooperative agreement with FDA.
8	Creating a National Surveillance Infrastructure for Devices Used in Hernia Repairs	Mesh for ventral hernia repair	New York State's Department of Health's SPARCS and Abdominal	Long-term catastrophic complications including hernia recurrences, hospital	None	Ongoing	737 registry patients	A 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
			Core Health Quality Collaborative	readmissions, reoperations, surgical site infections, and mesh-related complications				
9	Active Surveillance of Medical Device Safety and Outcomes Using electronic health records (EHRs): Prostate Cancer Partial Gland Ablation Technologies	Prostate Cancer Partial Gland Ablation Technologies	Electronic Health Records (EHRs) at Weill Cornell Medicine	Data elements harvested from EHRs into Natural Language Processing and High-Performance Integrated Virtual Environment repository that are integrated into Study of Prostate Ablation Related Energy Devices (SPARED) registry	None	Ongoing	111 Patients	A cooperative agreement with FDA.
Completed/Terminated/Discontinued Projects from Previous Reports								
	Signal Detection: Opioid Use and Risk of Joint Revision Surgery	Total knee and total hip	Kaiser Permanente's Total Joint Replacement Registry and	Risk of revision surgery	Johnson & Johnson, Smith & Nephew, and Zimmer Biomet	Completed	24,105 (knees) 12,895 (hips)	A 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
			EHRs					
	Data Extraction and Longitudinal Trend Analysis (DELTA)-ICD leads	Implatable cardioverter defribillator (ICD) leads	ICD Registry in the National Cardiovascular Data Registry	Survival (freedom from failure)	None	Completed	374,132	A cooperative agreement with FDA.
	SPARED Robot-Assisted Cystectomy	Robotic devices	Surveillance, Epidemiology, and End Results - Medicare data	Benign ureter stricture and stricture diagnoses	None	Completed	1,781 patients	A cooperative agreement with FDA.
	Women's Health Technology (WHT)-Coordinated Registry Network (CRN) mesh for Pelvic Organ Prolapse (POP) repairs	Mesh implants used in pelvic organ prolapse repairs	New York State's Department of Health's SPARCS	Reoperation risk	None	Completed	54,194 patients	A cooperative agreement with FDA.
	WHT-CRN slight mesh for Stress Urinary Incontinence (SUI)	Sling mesh implants for stress urinary incontinence	New York State's Department of Health's SPARCS	Reoperation and erosion	None	Completed	36,195 patients	A cooperative agreement with FDA.
	Outpatient Surgical Procedures for the Treatment of Benign Prostatic Enlargement in	Transurethral prostatectomy and laser prostatectomy	New York State and California statewide databases	Reoperation rates	None	Completed	85,682 men	A 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
	New York State and California							
	VISION	Stents, stent-grafts, and other devices used in the treatment of diseases of the peripheral circulatory system	VQI-Medicare data, New York State Department of Health's SPARCS, device manufacturer clinical trial databases	Death, procedure-specific adverse events (stroke, rupture, and amputation), reinterventions, readmissions, surveillance, imaging, cost	Cook Medical, Endologic, W. L. Gore & Assoc., and Medtronic	Completed	>300,000 patients	A cooperative agreement with FDA.
	Orthopedics Coordinated Registry Network (Ortho CRN) formerly named *ICOR-USA*	Joint replacements	Orthopedics Coordinated Registry Network members: Kaiser Permanente, American Joint Replacement Registry , Function and Outcomes Research for Comparative Effectiveness in Total Joint Replacement Registry, and Michigan	Revision rates	Zimmer Biomet, Smith & Nephew, and Johnson & Johnson	Completed	>600,000 patients	A 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
			Arthroplasty Registry Collaborative Quality Initiative					
	VQI-DELTA PTX Study	PTX Drug-Coated Balloons and PTX Drug-Eluting Stents	VQI data collected by the Society of Vascular Surgeons	Survival (i.e., freedom of death from any cause)	Medtronic, Bard, Philips, Cook, and Boston Scientific	Completed	7,814 patients	A cooperative agreement with FDA.
	Outpatient Surgical Procedures for the Treatment of Benign Prostatic Enlargement in New York State and California	Transurethral prostatectomy and laser prostatectomy	New York State and California statewide databases	Reoperation rates	None	Completed	85,682 men	A cooperative agreement with FDA.
	Evidence-Based Objective Performance Criteria (OPC) for the Evaluation of Hip and Knee Replacement Devices and Technologies	Total Hip Arthroplasty and Total Knee Arthroplasty devices	Literature, Function and Outcomes Research for Comparative Effectiveness in Total Joint Replacement Registry, Kaiser Permanente Registry, the New York State Department of	Patient-Reported Outcome Measures and cumulative joint revision rates at 2 years	None	Completed	653,662 patients	A 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
			Health's SPARCS, and the California OSHPD					
	EVAR Conversion	Endovascular Treatment Devices	VQI-Medicare linked dataset for EVAR	In-hospital mortality, 30-day mortality, 1-year mortality, length of Stay, Intensive Care Unit length of stay, hospital readmission within 30 days, and discharge destination	None	Completed	15,937 EVAR patients	A cooperative agreement with FDA.
	DELTA-Transcatheter Aortic Valve Replacement (TAVR)	Aortic and mitral valves	National Cardiovascular Data Registry Transcatheter Valve Therapy Registry	Survival (i.e., freedom from a composite of death, stroke, or repeat valve operations)	Medtronic, Abbott, and Edwards	Discontinued	> 150,000 patients	A cooperative agreement with FDA.
	WHT-CRN Urogynecological Mesh and Risk of Cancer	Mesh	New York State's Department of Health's SPARCS	Cancer	None	Discontinued	59,117 patients	A cooperative agreement with FDA.