Report to Congress

Device Pilot Projects
under
Section 708 of the Food and Drug Administration Reauthorization Act of 2017
which amended
Section 519 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360i)

U.S. Department of Health and Human Services

Food and Drug Administration

Executive Summary

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

The law 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 is understood relative to traditional or "passive surveillance," whereby an active approach relies on users to proactively notify FDA of device-related events (e.g., adverse event reporting). For purposes of 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 (CDRH) at FDA has documented an increase in the use of real-world evidence (RWE) to support regulatory decision making. The use of RWE may be less burdensome for manufactures because it is often less costly and can generate meaningful information about the safety and effectiveness of devices in a more timely manner than traditional studies.

The law 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 an 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, and urogynecological 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, the 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 future work outlined here will increase the scale and impact of these capabilities.

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Acronyms used in this report

ACC	American College of Cardiology
CDRH	Center for Devices and Radiological Health
CI	Confidence Interval
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
FDA	Food and Drug Administration
FDARA	FDA Reauthorization Act
FORCE	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
MARQI	Michigan Arthroplasty Registry Collaborative Quality Initiative
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
PAS	Postapproval Study
PCORTF	Patient-centered Outcomes Research Trust Fund
POP	Pelvic Organ Prolapse
RWD	Real-world Data
RWE	Real-world Evidence
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) ("Device Pilot Projects") amended section 519 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360i). The law requires the Secretary of Health and Human Services (HHS) to provide a report to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor, and Pensions of the Senate containing a description of the pilot projects being conducted, and projects continued or expanded, pursuant to section 708 of FDARA.

II. Background on FDARA and 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 is understood relative to traditional or "passive surveillance," whereby an active approach relies on users to proactively notify FDA of device-related events (e.g., adverse event reporting). For purposes of 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 includes:

- Ongoing systematic monitoring of an existing high-quality granular data source with regular feedback regarding safety alerts to the manufacturer and regulators.
- Postmarket safety 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 efficacy and durability.
- 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 the legislation. 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.

As intended by the law, this report has been prepared to contribute to the independent third-party evaluation of the strengths, limitations, and appropriate use 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 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 (CDRH) at FDA has documented an increase in the use of RWE to support regulatory decision making. The use of RWE may be less burdensome for manufactures because it 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 these device types may be associated with significant health consequences. The pilots involve devices and device types for which the collection and analysis of RWE regarding a 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, transcatheter heart valves, peripheral vascular implants, and urogynecological mesh. Several of these projects are already producing RWE for device evaluation (premarket and postmarket) by various stakeholders, including FDA and industry. In addition, the 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 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. Method of Pilot Project Description

The law 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 April 2018)

Involvement of the manufacturer is broadly defined and inclusive. Some of the projects have 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 pilot projects that are under development but not yet operational. Section VI presents pilot projects that are more mature and contributing to active surveillance.

A note about Coordinated Registry Networks (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. Developmental 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 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 post-surgical 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 the 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 increased risk of total joint revision surgery and whether it can be used as an early signal in active postmarket surveillance of devices.

Data source(s): KP total joint replacement registry and KP's EHRs.

Safety outcome(s) of interest: The outcome of interest was risk of revision surgery.

Numbers and names of manufacturers involved: Three manufactures 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:
TKA findings:
The findings of this project have been published.[1] 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 mg), medium-high (220-533 mg), and high (≥ 534 mg). Compared to patients not taking any opioids, patients using medium-low to high OME after the initial 90-day period had a higher adjusted risk of 1-year revision, ranging from a hazard ratio = 2.4 [95 percent confidence interval (CI), 1.3-4.5] to a hazard ratio = 33 (95 percent CI, 10-110) depending on the OME and time period.

THA findings:
The findings of this project have been published.[2] 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 91-180 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 181-270 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.

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[1] 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):331-336. doi: 10.1016/j.arth.2017.09.001. Epub 2017 Sep 13.

[2] 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. doi:10.1080/17453674.2016.1181820

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

Status:
The first phase of these pilot projects has been completed, demonstrating proof-of-concept. The next phase of the pilots will assess generalizability of these methods to other devices and healthcare environments. The second phase is being planned.

2. Project name: EP PASSION (Electrophysiology Predictable and Sustainable Implementation of National) Registries – Methods to replace traditional post-approval studies

Description: EP PASSION is an on-going pilot project that is developing methods to replace traditional mandated post-approval studies (PAS) with active surveillance. Implantable cardioverter defibrillator (ICD) leads and cardiac re-synchronization therapy (CRT) device leads are involved in this pilot project. Current PAS of high voltage ICD and CRT leads are conducted in prospective new patient enrollment studies. The current approach is costly, requires years to complete enrollment, and does not always maintain sufficient patients for follow-up. This proposal aims to reduce study cost, duration, and attrition 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 being planned by a consortium of voluntary stakeholders and requires no funding from the FDA. The funds for the conduct of the pilot will come from the manufacturers involved, and the American College of Cardiology (ACC) will conduct the pilot.

Specific aim(s): The aims for the four phases of the pilot project and anticipated durations are:

Phase 1 (Current): Identify minimal set of core data elements for assessment of pacing and defibrillation leads.

Phase 2: Determine existing sources of data, which may require formation of several working groups (6 months).

Phase 3: Develop method to collect core data elements not available from existing data sources (12 months).

Phase 4: Develop linked approach to combine data elements from sources identified or created in Phases 2 and 3 (12 months).

Peri-procedural and lead/device revision data collection is important for development of the platform for future use in premarket submissions and for devices requiring additional data to be collected postmarket (e.g., leadless pacemakers).

Data source(s): This pilot project includes: administrative claims, device remote monitoring data, product registration records, and a national device registry.

Safety outcome(s) of interest: Outcomes include cardiac tamponade, cardiac perforation, lead dislodgement, loss of capture, abnormal pacing impedance, abnormal defibrillation impedance, insulation breach, and lead/conductor fracture.

Numbers and names of manufacturers involved: The five manufacturers involved in the pilot include: Abbott, BIOTRONIK, Boston Scientific, LivaNova, and Medtronic.

Number of patients: The number of patients has not yet been determined.

Findings of project: Not available currently

Status: Ongoing

The EP PASSION pilot project is ongoing. Technical work completed to date includes agreement on core minimum data sets, standards for data quality, and methods for linking registry with outcomes data (such as claims).

VI. Production Pilot Projects

A. DELTA - ICD (implantable cardioverter defibrillator) leads and TAVR (transcatheter aortic valve replacement)

The DELTA (Data Extraction and Longitudinal Trend Analysis) 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. DELTA can simultaneously support multiple prospective analyses, permitting the system to monitor the safety of multiple device-outcome pairs in a continuously growing data set.

DELTA is being tested and implemented in several data systems. Two of the projects are described here.

1. Project name: DELTA-ICD leads

Description: Over the past several 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 is being conducted by Lahey Hospital and Medical Center and Tufts University School of Medicine under a cooperative agreement with FDA and a grant from the William Wood Foundation.

Specific aim(s): This pilot project is to validate a strategy for automated active safety surveillance of contemporary high-energy ICD leads based on prospective, propensity-matched survival analysis.

Data source(s): ICD Registry in ACC's National Cardiovascular Data Registry (NCDR). Existing DELTA server/software installed at ACC is used for the analysis.

Safety outcome(s) of interest: The freedom from failure is the key outcome in this study. Proposed analyses will be performed using definitions provided by NCDR to maximize consistency of outcome and clinical covariate definitions.

Numbers and names of manufacturers involved: These devices are produced by four companies: Guidant/Boston Scientific, Medtronic, Sorin Group, and St. Jude Medical. The plan is to include industry on the Steering Committee.

Number of patients involved: The pilot project includes 630,847 patients, which represents almost all ICDs implanted in the United States.

After approval of the study protocol, and before any case-level ICD Registry data is made available to DELTA, the study will be registered on ClinicalTrials.gov and the protocol will be made available through the DELTA research website. All analyses specified in the final protocol will be considered "pre-specified." Findings anticipated for the pilot include the relative safety of several ICD leads which have, to our knowledge, not previously been analyzed using comparative safety techniques.

Findings of project: None currently

Status: Ongoing

2. Project name: DELTA-TAVR

Description: Recently, transcatheter-based techniques have evolved to allow aortic valve replacement without the need for open sternotomy or cardiopulmonary bypass. In 2012, the Society of Thoracic Surgeons (STS) and ACC launched the STS/ACC Transcatheter Valve Therapy (TVT) Registry, a national program to evaluate the safety and effectiveness of TAVR. Automated, active, prospective surveillance of the TVT registry may allow early identification of potential safety issues associated with the use of FDA-approved TAVR devices.

Party conducting the pilot project and agreement type: This pilot project is being conducted by Lahey Hospital and Medical Center and Tufts University School of Medicine under a cooperative agreement with FDA and a grant from the William Wood Foundation.

Specific aim(s): This pilot project is to evaluate the relative safety of contemporary transcatheter aortic valve devices in TAVR procedures using automated active surveillance.

Data source(s): STS/ACC TVT Registry

Safety outcome(s) of interest: Outcomes of interest are survival (freedom from a composite of death, stroke, or repeat valve operations).

Numbers and names of manufacturers involved: Three manufactures are involved as members of the stakeholder advisory committees: Edwards Life Sciences, Medtronic, and Abbott.

Number of patients involved: Currently there are over 150,000 patients enrolled in the TVT registry.

Findings of project: None currently

Status: The pilot will start pending final approval by the TVT Research and Publication Committee and the TVT Steering Committee.

B. Surveillance Efforts via Established CRNs

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

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, validation of complications, and support risk adjustment of outcomes.

Party conducting the pilot project and agreement type: The pilot project is being led by 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: 1) to 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 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): Data sources for this pilot project include: 1) Society for Vascular Surgery (SVS) Vascular Quality Initiative (VQI) Registry; 2) Medicare claims; 3) SPARCS (New York's Statewide Planning and Research Cooperative System); and 4) device manufacturer clinical trial datasets. 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: Primary outcomes identified in linked datasets include: death, procedure-specific adverse events (stroke, rupture, and amputation), re-interventions, readmissions, and surveillance imaging.

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

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

Findings of project: Initial VISION efforts focused on validation of claims data to capture outcomes of interest. For example, in one of the studies involving endovascular aortic repair, 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.[3]

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 follow-up of patient outcomes.[4]

Building on these efforts, a propensity-matched study was conducted comparing long-term survival of carotid artery stenting and carotid endarterectomy. In contrast to randomized clinical trial findings, this CRN study demonstrated survival advantage of stenting over endarterectomy in real-world practice. [5]

Registry-linked datasets have been created for nine procedures. New devices are being added as they are approved or cleared for market in the U.S.

Status: The pilot is currently operating and being updated annually.

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[3] 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. 2018;1-6. doi: 10.1016/j.jvs.2018.03.423.

[4] 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;66:751-9.

[5] 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. 2018;1-6. doi: 10.1016/j.jvs.2018.03.432.

2. Project name: ICOR (International Consortium of Orthopedic Registries) USA

Description: The ICOR-USA pilot project seeks to apply lessons learned from the ICOR to improve clinical evidence generation and safety evaluation for orthopedic implants in the U.S. via creation of a strategically coordinated registry network (Ortho CRN).[6]

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 U.S. based data sources: KP, the American Joint Replacement Registry, the Function and Outcomes Research for Comparative Effectiveness in Total Joint Replacement Registry (FORCE), and the Michigan Arthroplasty Registry Collaborative Quality Initiative (MARQI).

Safety outcome(s) of interest: Primary outcomes of interest for this pilot project are benchmarking performance metrics for hip and knee replacements.

Numbers and names of manufacturers involved: Three manufactures 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: NA currently

Status: Phase one of the pilot is to demonstrate the feasibility of the project; phase two will expand the pilot nationally pending funding.

C. Claims-based State Surveillance

The pilot projects described in this section use data from the state of New York. The Statewide Planning and Research Cooperative System (SPARCS) is a comprehensive all-payer data reporting system that collects discharge data from New York hospitals. SPARCS currently collects patient-level detail on patient characteristics, diagnoses and treatments, services, and charges for each hospital inpatient stay and outpatient (ambulatory surgery, emergency department, and outpatient services) visit; and each ambulatory surgery and outpatient services visit to a hospital extension clinic and diagnostic and treatment center licensed to provide ambulatory surgery services.[7]

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[6] Etkin CD, Springer BD. The American Joint Replacement Registry—the first 5 years. *Arthroplasty Today*. 2017;3(2):67-69. doi:10.1016/j.artd.2017.02.002.

[7] Statewide Planning and Research Cooperative System (SPARCS). Available at: https://www.health.ny.gov/statistics/sparcs/ Accessed on May 29, 2018.

Project name: Urogynecological mesh and cancer

Description: The pilot project worked to determine if there was a potential link between synthetic polypropylene mesh implantation for transvaginal POP (pelvic organ prolapse) and SUI (stress urinary incontinence) and carcinogenesis. The use of mesh to reinforce weak tissue has been part of surgical intervention since the 1940s. Beginning in the late 1990s, synthetic mesh was first cleared for use in women with POP and SUI. The use of mesh for POP has been reclassified to a Class III device.[8,9]

Party conducting the pilot study and the agreement type: The pilot project was conducted by Weill Cornell School of Medicine under a cooperative agreement with FDA. This pilot worked with stakeholders including the American Uro-gynecological Society.

Specific aim(s): The first phase of the pilot aimed to demonstrate the feasibility of using claims data for cancer surveillance; the second phase is intended to implement the work nationally, pending identification of funding.

Data source(s): The data source used in this project is SPARCS—a comprehensive all-payer data reporting system that collects discharge data from New York hospitals.[10]

Safety outcome(s) of interest: The primary outcome is development of cancer at 1, 2, and 3 years, and during the entire follow-up.

Numbers and names of manufacturers involved: No manufacturers are involved in this pilot project.

Number of patients involved: Data from 59,117 patients were used in this pilot.
A total of 2,229 patients who underwent mesh-based POP surgery and 10,401 who underwent sling surgery for SUI between January 2008 and December 2009 were included in the study. The control cohorts included 40,007 women treated with cholecystectomy and 6,480 treated with vaginal hysterectomy. Mean follow-up was 6 years (range 5 to 7). Exact matching between the mesh and control cohorts was used to reduce bias.

Findings of project: Based on the findings from this data collection, transvaginal mesh was not associated with an increased risk of a cancer diagnosis (pelvic/local cancers or any cancer) at 1 year and during the entire follow-up of up to 7 years.

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[8] Reclassifying transvaginal prolapse mesh from class II to III: https://www.federalregister.gov/documents/2016/01/05/2015-33165/obstetrical-and-gynecological-devices-reclassification-of-surgical-mesh-for-transvaginal-pelvic

[9] Calling for PMAs for transvaginal prolapse mesh: https://www.federalregister.gov/documents/2016/01/05/2015-33163/effective-date-of-requirement-for-premarket-approval-for-surgical-mesh-for-transvaginal-pelvic-organ

[10] Statewide Planning and Research Cooperative System (SPARCS). Available at https://www.health.ny.gov/statistics/sparcs/ Accessed on May 29, 2018

Status: The pilot demonstrating feasibility is complete. Pending identification of funding, a second phase to expand the effort nationally is being planned.[11]

VII. Other Potential Pilot Projects

Additional pilots that promote active surveillance have been planned or are in the process of development. Two potential pilot projects are listed here based on CRNs that are currently being established. These CRNs are in the early stages of development, but will include active surveillance as a capability.

A. Women's Health Technology CRN

Numerous safety signals involving medical devices used as part of obstetrics and gynecology have been documented, including urogynecological mesh, morcellators, and permanent sterilization devices. A Women's Health Technology CRN is being developed with funding from the PCORTF (Patient-Centered Outcomes Research Trust Fund). A broad group of stakeholders, including patient groups, device manufacturers, professional societies, and federal agencies, has been convened to support the development of this CRN. The CRN is in the early stages of development, and data sources have not been finalized. Active surveillance is planned as part of this CRN.

B. SPARED (Study of Prostate Ablation Related Energy Devices)

Several devices are being used for ablation of prostate tissue including ultrasound, cryotherapy, and nanoparticles to heat tissue. A CRN has been proposed to address the need for ongoing evaluation of these devices as they relate to tissue ablation to treat prostate cancer. A series of meetings has brought together the stakeholders to plan the development of this CRN. This CRN is in an early stage of development. Active surveillance is planned to be included in this CRN. Currently, data sources have not been identified for this effort.

VIII. 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 future work outlined here is intended to increase the scale and impact of these capabilities.

[11] Chughtai B, Sedrakyan A, Mao J, Thomas D, Eilber KS, Clemens JQ, Anger JT. Challenging the myth: transvaginal mesh is not associated with carcinogenesis. The Journal of Urology. 2017 Oct;198(4):884-9.

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	Number of patients	Agreement type
1	Signal detection: Opioid use and risk of joint revision surgery	Total knee Total hip	Kaiser Permanente Total Joint Replacement Registry and EHR	Risk of revision surgery	Johnson & Johnson, Smith & Nephew, Zimmer	Phase 1 complete, Phase 2 planned	24,105 (knees) 12,895 (hips)	Cooperative agreement with FDA.
2	EP PASSION	Implantable cardioverter defibrillator and cardiac re-synchronization therapy leads	Administrative claims, device remote monitoring data, product registration records, national device registry	Cardiac tamponade and perforation, lead dislodgement, loss of capture, abnormal pacing and defibrillation impedance, insulation breach, lead or conductor fracture	Abbott, BIOTRONIK, Boston Scientific, LivaNova, Medtronic	Planning	Not yet determined	No funding for the first phase. Funding from industry for next phase.
3	DELTA-ICD	Implantable cardioverter defibrillator leads	NCDR ICD Registry	Survival (freedom from failure)	No formal involvement yet-plan to include industry on the steering committee	Ongoing	630,847	Cooperative agreement with FDA and funding from William Wood Foundation.
4	DELTA-TAVR	Aortic and mitral valves	NCDR TVT Registry	Survival (freedom from a composite of death, stroke, or repeat valve operations)	Medtronic, Abbott, Edwards	Pending approval by TVT committees	>150,000	Cooperative agreement with FDA.
5	VISION	Stents, stent-grafts, and other devices used in treatment of diseases of the peripheral circulatory system	VQI Registry, Medicare claims, SPARCS	Death, procedure-specific adverse events (stroke, rupture, and amputation), reinterventions, readmissions, and surveillance imaging	Cook, Endologic, Gore, Medtronic	Completed, updated annually	~300,000	Cooperative agreement with FDA; seeking funding from industry for next phase.
6	ICOR-USA/Ortho CRN	Joint replacements	KP Registry, American Joint Replacement Registry, FORCE, MARQI	Complication rates	Zimmer, Smith & Nephew, Depuy	Phase 1 is on-going; Phase 2 being planned	>1,862,658	Cooperative agreement with FDA.