NEST Coordinating Center
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Posting Date: July 17, 2023
Indication of Interest: July 26, 2023
Due Date: August 28, 2023

Request for Proposal 23-AS1001

NESTcc Medical Device Active Surveillance – Central Data Operations Hub

Key Dates

Key Dates	
Request for Proposal Released	July 17, 2023
Deadline for Questions	July 21, 2023
Indication of Interest	July 26, 2023
Responses to Questions	July 31, 2023
Deadline for Proposals	August 28, 2023
Projected Notification of Interest in Presentation	September 1, 2023
Presentation of Proposals	September 11-12, 2023
Projected Notification of Selection Date	September 18, 2023
Projected Start Date	September 30, 2023

Overview

This Request for Proposal (RFP) is part of an ongoing collaboration between the Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH) and the National Evaluation System for health Technologies (NEST) Coordinating Center (NESTcc) and focuses on the Central Data Operations Hub for the Active Surveillance Program for medical devices. [1]

NESTcc and FDA intend to develop and implement an active surveillance system of electronic health data to better understand the safety of medical devices as used within clinical practice. Once realized such a system will optimize data collection, quality, completeness, and analysis within a comprehensive framework to assess potential and ongoing safety signals in a timely manner. The active surveillance program is focused around achieving better data capture, detection of potential safety signals, and a timely assessment leading to actionable findings. In addition, the data structure developed for the active surveillance system will be viable for generation of real-world evidence fit for purpose for regulatory decisions.

[1] This project will be supported by a sub-award from Federal Award Identification Number (FAIN) U01FD006292.

NESTcc Background

NEST was established in 2016 by a cooperative agreement between the FDA's CDRH and the Medical Device Innovation Consortium (MDIC), a 501(c)3, the first public-private partnership created with the sole objective of advancing regulatory science of medical devices for patient benefit. The purpose of NESTcc is to increase quality and efficiency in the development of real-world evidence (RWE) to inform medical device development and evaluation, as well as support clinical, patient, regulatory, and reimbursement decisions throughout the total product lifecycle (TPLC).[2] NESTcc catalyzes RWE generation for medical device and health technology for all members of the device ecosystem. One of the specific aims of the agreement is to develop new systems of data collection and/or analysis to permit prospective active medical device post-market risk identification.

NESTcc Role

As described in the FDA's Medical Device Safety Action Plan: Protecting Patients, Promoting Public Health, NEST is intended, in part, to be an active surveillance and evaluation system that complements the passive surveillance approaches currently in use. FDA's current reliance on more traditional surveillance studies can take a long time before we can characterize any risks and determine whether a signal represents a true safety concern. By driving standardization of data capture, quality, and completeness by electronic health information owners; by establishing agreements with those data owners for efficient data access; and by providing for the linkage and aggregation of large data sets to which advanced methods and analytics can be applied prospectively, NEST will facilitate detection of potential safety risks that would not otherwise have been identified as quickly, or at all, as well as facilitate more timely assessment of potential safety signals. In doing so, NEST also will provide for data that better capture the safety and effectiveness of devices across diverse populations and across the range of clinical settings, allowing for better device evaluation pre- and post-market. [3]

From 2019 – 2022, NESTcc and its stakeholders, including the FDA, collaborated closely to plan an active surveillance environment for medical device safety. During this period, NESTcc formed the Active Surveillance Task Force; established multiple Working Groups; completed the setup and testing of a pilot analysis (Phase I) within a cloud-based environment followed by the simulation, development, and testing of a pilot federated cloud environment along the issuance of a draft Active Surveillance Road Map. The decision has been made with the FDA to continue investment in building an Active Surveillance program and has resulted in the issuance of this RFP.

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[2] National Evaluation System for health Technology coordination center (NESTcc). About https://nestcc.org/about/about-us/

[3] Medical Device Safety Action Plan: Protecting Patients, Promoting Public Health. https://www.fda.gov/media/112497/download

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Project Concept

Background

This solicitation is for a contract to develop and execute a minimally viable medical device active surveillance system in collaboration with NESTcc and the FDA. Key aspects of this medical device active surveillance system include:

- **Detection** of potential signals without comparisons between devices
- **Notifying FDA** of a potential signal, including the ability to share de-identified event- and patient-level information with the FDA, when requested by the FDA
- Continued data accrual and **monitoring** of devices over time, including conduct of replicate analyses despite changes in source records (at least monthly)

Active Surveillance Infrastructure

Active surveillance utilizes extant electronic health data to assess the safety of medical products. It does not require collection of new data from patients or clinicians, nor does it require that separate safety reports be generated and sent to the monitoring entity.

Many active surveillance systems utilize distributed data networks in which multiple institutions retain individual patient health data behind their own firewalls, execute standardized assessments using a common data model, and share aggregated results. Governance and infrastructure vary across distributed data networks, however most use a federated data exchange to minimize data sharing and a common data model to maximize on efficiency and resources while conducting repetitive queries for safety monitoring. Such networks maintain patient privacy while utilizing infrastructure and information sharing to assess public health and medical product safety in a sustainable manner.[4]

While many distributed data networks exist, there has been limited realization of utility for medical device surveillance. This may be due to the **depth of procedural data needed to adequately identify device use** and subsequent safety coupled with the breadth of data needed to assess the longevity of effects (e.g., implants remain in the body for decades). Additionally, differing data capture is needed across therapeutic areas to understand the safety of devices. A device-focused system is warranted to address these needs.

Many distributed data networks focus on signal refinement – characterizing the potential impact of a safety signal. **For medical devices, a primary need for an active surveillance system is signal detection** – identifying new potential risks or changes in known risks that may affect the benefit-risk profile. The methodologies and applications for signal detection differ from signal refinement, and a device-focused system is needed for identification of potential signals.

FDA made an initial investment in active surveillance in a cooperative agreement with the National Evaluation System for health Technology coordinating center (NESTcc) in April 2019 to develop an active

[4] Tabano DC, Cole E, Holve E, Davidson AJ. JPHMP 2017;23(6):674-83.

surveillance system capable of detecting potential safety "signals" for death, reintervention, or rehospitalization associated with medical devices. This initial work included simulation, development, and testing of a pilot federated cloud environment and issuance of a draft Active Surveillance Roadmap. Lessons learned from the initial investments will be leveraged to provide continued monitoring of electronic health data to quickly identify new potential signals and changes in frequency for known potential signals for marketed medical devices.

Objective

Expanding on previous work, this solicitation is to establish the central data operations "hub" of a medical device active surveillance system distributed data network. The central hub will work with data partners (identified by NEST, though proposals including ongoing data partnerships will be considered) with sufficiently linked medical claims and electronic health records (EHR) and other electronic health data to capture all medical encounters over a period of at least 1 year for U.S. patients and with sufficient granularity to capture brand and version (ideally via Unique Device Identifier [UDI]). The selected vendor will serve as the central hub and will be responsible for designing the initial version of the active surveillance system, developing the system, and providing day-to-day system operations.

The active surveillance system should use privacy-preserving and (horizontal) federated learning techniques in a cloud-based environment to monitor (primarily) for signal *detection* using containerized analytic modules distributed to data partners for execution against data in a common data model (or alternatively, using FHIR-based interoperability between data sources). In addition to facilitating governance and day-to-day operation for standardized data curation and analytics, the central hub will contribute to establishing best practices and prioritizing enhancements for data architecture, IT systems and infrastructure, patient privacy and ethics, and active surveillance methodologies.

Scope

The work required for this requirement can be broken down into three areas:

- Designing and developing an active surveillance system;
- Maintaining the active surveillance platform infrastructure, security, and data privacy; and
- The implementation and day-to-day operations to conduct active surveillance within the system.

The design and development of a system may depend on the types of devices being monitored. NESTcc and FDA are interested in someday including implanted devices, capital equipment, single use devices, and ongoing use of durable medical equipment within the active surveillance system. The two proof of concept use cases will be finalized at the time of contract. For the purposes of this solicitation, the following two cases will be considered:

- Duodenoscopes (including fully disposable, disposable components, and reprocessed duodenoscopes)
- Devices used in cholecystectomy procedures
    - High-priority – laparoscopes, robotically assisted surgical devices (RASD), energy systems
    - If available – trocars, closure devices, suction/irrigation devices, insufflation devices, hand access instruments)

Organizational Configuration

NESTcc anticipates an active surveillance system organized by a vendor that must:

- Ensure adequate governance to guide development and utilization of the system;
- Develop and maintain a culture of protecting patient privacy while obtaining actionable evidence for device safety; and
- Increase workflow efficiencies through continual data, architecture, and process improvements.

Eligibility

This opportunity is open to private-sector, nonprofit, and for-profit organizations, especially those with experience in surveillance methodologies as well as implementation of a federated health data system (e.g., governance and infrastructure, IT and security, development of containerized modules deployed from a single central hub to multiple data holders, allowance for identification and sharing of encrypted data for individuals across data sources, using interoperability [via FHIR or CDM] to enhance collaboration and automation, retrieval of output from behind data holder firewalls, and aggregation and deployment of synthesized results via application program interface [API]).

Details and Requirements

Scope of Work

The proposal **must not exceed 15 pages** and should include a plan for development and implementing the following:

(1) Design and Develop Active Surveillance System Infrastructure
  - Identify and gather system specifications, including infrastructure for data sharing across a federated network and aligned with the requirements outlined in Attachment 1
  - Architect a distributed data network capable of performing distributed and federated analyses via packaged analytics sent from a central scientific operations center to data partner sites and receipt of results from partner sites for aggregation by the coordinating center – the design should establish standardized systems, quality control, and use of a common data model to assure interoperability
  - Develop distributed data network which meets all requirements outlined in Attachment 1 and design specifications
    - NOTE: System design, build and updates anticipated to follow principles of agile IT development, with sign-off of initial requirements followed by iterative development and testing via sprints. NESTcc and FDA to provide sign-off between pre-defined stages (based on pre-defined work plan).
  - Establish and implement systems, quality control, and validation tests to confirm interoperability of data between sites

- Develop, deploy, and test federated learning within the network such that training/modeling occurs behind site firewalls and parameters are provided for aggregation to the central hub
- After initial testing of active surveillance with first device (see #4 below) modify system specifications and architecture
- Update infrastructure build to minimally viable ongoing active surveillance system
- Prioritize initial build and updates

(2) Governance, Oversight, Security, Privacy
- Establish governance structure and oversight
- Establish end-to-end processes for conduct of active surveillance projects (including descriptive queries, determining background rates, serial monitoring, and complex comparisons), onboarding and integrating new data partners, prioritizing new active surveillance efforts, engaging new partnerships for active surveillance methodologies and infrastructure other than data, and garnering input from medical device ecosystem
- Establish and execute security and compliance plan
- Develop high-priority SOPs/policies, especially regarding security and patient privacy

(3) Data Partners
- Set-up and validate at least two (2) and up to six (6) data partners' health data as site within active surveillance system (developed in #2)

(4) Active Surveillance Analysis with First Device
- Develop protocol and analytic plan for active surveillance analysis
- Obtain IRB approval or exemption
- Develop NLP/tokenization (or other identification) for device and outcome(s) for first device area, as needed
- After initial infrastructure build (see item #2), conduct initial review/testing of first device active surveillance
- After updates to generate minimally viable system (MVS) build, implement MVS active surveillance for first device
- Conduct analysis in accordance with protocol; report potential signals to FDA (e.g., via API)

(5) Second Device or COVID-19 specific device evaluation
- Develop protocol and analytic plan for analysis
- Obtain IRB approval or exemption
- Develop NLP/tokenization/AI/ML (or other) to identify device and outcome(s), and other data elements as needed
- Conduct analysis in accordance with protocol; report potential signals to FDA (e.g., via API)

(6) Provide feedback and contribute to stakeholder community development
   - Provide feedback on AS Roadmap
   - After initial testing of active surveillance with first device (see #4 above), discuss and confirm lessons learned for future AS modules and devices
   - Contribute to planning for ongoing maintenance and system upgrades to scale for multiple ongoing surveillance efforts

Submission Components

Applications must be submitted via Smartsheet through the required format by 5p.m. EST on Monday, August 28, 2023. The application must include all required components listed below.

To enable NESTcc to evaluate the submission, the responding proposal must include the following:

1. A plan to establish the central data operations "hub" of a medical device active surveillance system distributed data network. The plan must comply with the guidelines outlined above and not exceed 15 pages.
2. A timeline for completing the required deliverables and key milestones within the period of performance
3. A proposed budget that includes proposed hourly rates for all personnel who will be supporting the project, as well as expected costs and expenses based on a timeline of meeting key milestones
4. Curriculum Vitae (CVs) of potential investigators and prior experience conducting similar engagements (experience with medical device evidence preferred)
5. Up to 3 Letters of Support from references demonstrating relevant capabilities required to perform the work outlined in this RFP

Period of Performance

September 30, 2023 – April 30, 2024

Deliverables to be Completed within the Period of Performance

NESTcc staff and FDA will approve each of the following deliverables and interim deliverables. These deliverables represent a minimum set of required deliverables. Additional deliverables can be proposed within the application.

Deliverable	Associated Interim Deliverables
1. Workplan outlining project approach	a. Draft workplan b. Updated draft workplan c. Final workplan
2. Implementation plan	a. Draft implementation plan (for sprints) b. Final implementation plan
3. Architecture and	a. Initial (high-level) draft architecture and workflow for system

specifications	b. Updated architecture c. Draft system requirements (including draft infrastructure/network configuration/ security/privacy/data refresh needs for data partners) d. Updated system requirements e. Draft build specifications f. Determination of preferred federated learning option g. Updated build specifications h. Final architecture (for minimally viable system for 1st AS device) i. Final system requirements (for minimally viable system for 1st AS device) j. Final build specifications (for minimally viable system for 1st AS device)
4. Governance charter	a. Draft charter b. Updated charter c. Final charter
5. Security and compliance plan	a. Draft security and compliance plan b. Updated security and compliance plan c. Final security and compliance plan
6. High-priority SOPs/policies	a. Draft prioritized list of SOPs/policies b. Final prioritized list of SOPs/policies c. Draft high-priority SOPs/policies d. Final (v1) high-priority SOPs/policies
7. Minimally viable system	a. FDA sign-off to initiate build (after #3e above) for 1st AS device b. FDA sign-off for alpha testing for 1st AS device c. FDA sign-off for beta/user testing (includeing NESTcc and FDA end users) for 1st AS device d. FDA sign-off to initiate build (after #3e above) for 2nd AS device e. FDA sign-off for alpha testing for 2nd AS device f. FDA sign-off for beta/user testing (includeing NESTcc and FDA end users) for 2nd AS device
8. Protocol and analysis plan for initial AS	a. Draft protocol and analysis plan (1st AS device) b. Final protocol and analysis plan c. Draft updated protocol and analysis plan (2nd AS device) d. Final updated protocol and analysis plan
9. IRB approval or exemption	a. Submission of IRB documentation b. Letter of IRB determination c. If needed, submission of updated IRB documentation (2nd AS device) d. If needed, updated letter of IRB determination (2nd AS device)
10. AS for 1st device	a. Device NLP/tokenization finalized b. Outcome NLP/tokenization finalized c. Analytic module draft d. Initial “quarterly” testing of module e. Initial “real-time” testing of module f. Analytic module final g. Confirmation of implementation of minimally viable system for AS

	within at least 1 data source
11. AS for 2nd device	a. Device NLP/tokenization finalized b. Outcome NLP/tokenization finalized c. Analytic module draft d. Completed testing of module e. Analytic module final f. Confirmation of implementation of minimally viable system for AS within at least 2 data sources
12. Incorporate data partners into AS system	a. Initial set-up of system requirements (including draft infrastructure/network configuration/ security/privacy/data refresh needs for data partners) for data partner #1 b. Testing with sample data c. QC and testing real data – analysis and transfer d. Final "onboard" and set-up complete for data partner #1 e. Onboard and set-up data partner #2 f. Onboard and set-up each data partner (plan for up to 6)
13. Participate in development of best practices	g. Provide feedback on AS Roadmap h. Participate in (up to monthly) meetings to develop best practices for medical device AS i. Participate in (up to two) meetings on lessons learned from first two AS devices

NOTE: NESTcc will be responsible for contracting with data partners, planning and implementing stakeholder engagement (including leading the finalization of the AS Roadmap)

Indication of Interest

As a preliminary step in the application submission process, please indicate your interest in submitting a proposal by contacting NESTcc@mdic.org by **5p.m. EST on July 26, 2023**. NESTcc will provide interested parties with any additional supplemental material to prepare the proposals no later than July 31, 2023.

Review Process

Responses to this RFP will be reviewed by NESTcc staff and FDA (Selection Team) through objective evaluation criteria. The Selection Team will select up to 10 proposals for presentation on September 11-12, 2023 (in person preferred, in the DMV). The responses and presentations will be considered by the Selection Team via objective evaluation criteria and the selected contractor will be informed.

NESTcc staff reserve the right to contact applicants with additional questions during the review period. NESTcc staff reserve the right to consult external stakeholders to review applications. Any external reviews will be completed in accordance with the MDIC conflict of interest policy. Responses will be reviewed for completeness and appropriateness of the responses as they pertain to the required submission components. NESTcc will consider both the programmatic aspects of the proposal, as well as the anticipated cost, with the programmatic elements of the proposal receiving greater weight. NESTcc may, for example, choose a costlier proposal if its programmatic offering warrants the premium.

However, as potential contractors' programmatic offerings move toward equivalency, cost will gain in importance.

NESTcc's selection of a contractor will be contingent on the parties executing a mutually acceptable contract on or before October 15, 2023. Because this project is funded with support from an FDA Cooperative Agreement, the contract will include all appropriate Federal terms and conditions, including but not limited to those found in 45 C.F.R. Part 75 and the HHS Grants Policy Statement, including any addenda thereto. NESTcc reserves the right to terminate contract negotiations at any time and select another contractor if it determines that it is unlikely that an agreement will be executed in a timely manner.

Timeline

- Posting Date: July 17, 2023
- Indication of Interest: July 26, 2023
- Due Date: August 28, 2023
- Presentation Date (by invitation): September 11-12, 2023
- Notification Date: September 18, 2023
- Contract Executed: October 15, 2023

NESTcc understands that questions may arise during the application process. Please send questions to NESTcc@mdic.org using the subject line "RFP 23-AS1001".

About MDIC

The Medical Device Innovation Consortium (MDIC) is the first public-private partnership created with the sole objective of advancing medical device regulatory science throughout the total product life cycle. MDIC's mission is to promote public health through science and technology and to enhance trust and confidence among stakeholders. We work in the pre-competitive space to facilitate development of methods, tools, and approaches that enhance understanding and improve evaluation of product safety, quality, and effectiveness. Our initiatives improve product safety and patient access to cutting-edge medical technology while reducing cost and time to market.

For more information visit: http://www.mdic.org

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Attachment 1 – Requirements

Active Surveillance System Requirements

Below are three areas necessary for success of the active surveillance system project: system infrastructure/build, operations, and governance. Requirements for each are provided.

System infrastructure/build

Functionality

- AS system applies advanced analytics to facilitate detection of safety signals
    - *Preferred*: System deployed to data partners through containers (modules) to minimize dependencies in the overall system when providing updates, modifications, or new deployments
- AS system utilizes a hub (central data operations hub) and spoke (local "nodes" at each data partner), cloud-based infrastructure to conduct and share analyses
    - *Alternate*: other system models *may* be considered during the proposal stage, with demonstration of increased analytic capabilities at no increase in budget, time, or other resources (compared with hub and spoke model)
- AS system consists of a distributed network of data partners
- AS system uses (horizontal) federated learning (or similar) to identify patients and attributes across multiple data partners' data sources, e.g., via tokenization
    - *Possible*: AS system uses (vertical) federated learning to identify new types of attributes across patients
- AS system utilizes "real-world data" from data sources (e.g., EHR, claims, and registries) updated at least monthly (though schedules may differ across data sources)
    - *Preferred*: RWD in AS system also includes patient generated health data, devices, pharmaceutical, supply chain, genomic, and other data collected outside of typical clinical trials
    - *Preferred*: Daily (or "real-time") updates to data sources
- Data within the AS system will be configured into a common data model and will support open APIs and FHIR standards
    - *Preferred*: OMOP common data model
    - *Alternate*: With demonstration of no increase in budget, time, or other resources and no loss of capability, a system reliant directly on HL7 FHIR standards will be considered.
- AS system will automate data cleansing and transformation including validation and quality checks of the associated processes
- AS system will centrally aggregate and monitor *results*

- AS system will port AS *results* for monitored devices (e.g., via API) to FDA each time data are updated

Data Partners

- Data partner environment must be capable of supporting the local occurrence/node of the AS system solution
- Data allows for generation of real-world evidence fit for purpose to inform total product lifecycle regulatory decisions, including EUA transitions
    - *Preferred*: Interface available for NESTcc and/or FDA to assess feasibility of new studies within at least one data source
- AS system will include US data partners
    - *Preferred*: Within two years of initiation, AS system would be capable of supporting non-US data partners

Patient privacy and compliance

- Patient-level data will remain behind a firewall in the data partner's environment during the AS evaluation (deidentified patient-level data may be sent to FDA upon identification of a potential signal during AS evaluation)
    - *Alternate*: If a data environment already exists, including established data use, security, and privacy agreements and established governance and workflows, alternate configurations will be considered. Demonstration of cost-effectiveness, scalability to other data sources, and patient privacy should be provided.
    - *Preferred*: Patient-level data may travel directly to FDA in the event of a signal or other need for direct evaluation by FDA
- Data partner must allow joining/communication of networks for (horizontal) federated learning between other data partner occurrences/nodes and central data operations hub network
    - If needed, firewall policies may be adjusted to allow traffic (e.g., for aggregated data) between central data operations hub and the data partner, with maintenance of patient privacy

IT/security

- AS system aligns with privacy and security standards
    - Minimally required: HIPAA, FISMA, ISO 27001, ISO 27701
    - Preferred (required within 2 years): ISO 13485, ISO 22301, benchmark to National Institute of Standards Technology
    - Preferred: GDPR, ISO 20000
- Access controls for each role of individuals interacting with the AS system will be established and maintained

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Operations

Workflow and tracking

- Project management, workflows, tracking, and communication are centralized
- The system will support an end-to-end audit trail of all workflows, including modifications to system
- The system will support an end-to-end audit trail of all modifications to data elements
- Planned periodic review and update will be established to provide process improvements

Reporting

- AS system will provide automated reporting of results
    - Preferred: Automated reporting includes visualization, is pushed to FDA via API, for integration with FDA dashboard(s)
- In the event of a signal, de-identified patient and event data can be provided to the FDA upon request

Scaling

- AS system will initially conduct analyses for detection of death, repeat procedure, and rehospitalization
    - AS system will be built with the intention for scaling to other outcomes
    - AS system will be built with the intention for scaling to refinement of signals
- Initial AS system includes at least two data partners
    - *Preferred*: at least six data partners and at least 10 million patients contributing at least one year of data
- Plan to scale such that within two years after initiation, AS system is capable of no fewer than 3 surveillance projects *in parallel* without service degradation
- Plan to scale such that within two years after initiation, AS system is capable of maintaining no fewer than 20 ongoing surveillance projects without service degradation

Active surveillance

- AS system will support active surveillance for novel pattern detection and unknown signals
    - *Preferred*: AS system will support suite of public health, medical product, and AI/ML-based methods for surveillance
    - *Preferred*: AS system will use federated analytics to conduct active surveillance
- AS system prioritizes signal *detection* activities
    - Note: AS system build should be performed such that signal *refinement* could be included in the future
- AS system prioritizes identification of signals *without* comparison of devices, procedures, products or therapies

- Note: Self-controlled analyses (e.g., self-controlled cohort, sequence symmetry) are not anticipated due to the outcomes planned for surveillance
- Note: Serial monitoring compared to threshold (e.g., control chart), previous time period with pre-determined inflection point (e.g., change point), and previous time period with data-driven inflection point (e.g., dynamic change point) are anticipated as the initial AS methods; proposals with alternative AS methods will be considered

Governance

- Governance will be established to guide AS system development, maintenance, and utilization
- Governance will be established to review and approve data access, security and privacy procedures, to review any events or near-misses, and to establish and enact corrective and preventative actions