The CBER Biologics Effectiveness and Safety (BEST) Initiative

Draft IDIQ Statement of Work (SOW)
June 2, 2017
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1. INTRODUCTION

1.1 BACKGROUND

The U.S. Food and Drug Administration (FDA) is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, tobacco products, our nation’s food supply, cosmetics and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines, devices, products, and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health. As part of its mission, the FDA conducts monitoring of the safety of regulated products.

In response to the FDA Amendments Act of 2007 (FDAAA 2007), the FDA established the Sentinel system and built a national electronic data system for monitoring the safety of FDA-regulated medical products. Sentinel is a distributed database system consisting of numerous data partners who retain operational control over their data within a secure environment; the Sentinel Operations Center manages, receives and processes FDA questions in the form of queries and returns summary results back to the FDA in a secure environment. The FDA Center for Biologics Evaluation and Research (CBER) established the Postlicensure Rapid Immunization Safety Monitoring (PRISM) system, within Sentinel, specifically to conduct studies and analyses of vaccine safety. CBER also established the Blood Safety Continuously Active Network (BloodSCAN) as an active postmarket system within Sentinel for evaluating the safety of blood and blood products. CBER uses the Sentinel system to conduct some of its epidemiological studies as part of its regulatory responsibilities.

However, CBER conducts a number of epidemiological studies outside of the Sentinel system. CBER’s Office of Biostatistics and Epidemiology (OBE) initiated postmarket safety studies working collaboratively with federal partners such as the Veterans Health Administration, Indian Health Services and Center for Medicare and Medicaid Services (CMS). In 2005, FDA initiated studies with CMS in the areas of vaccine and blood safety and in 2013 in vaccine effectiveness. For the last decade, FDA has worked collaboratively with CMS to institute ‘near real time’ surveillance or rapid cycle analysis (RCA) for Guillain-Barre Syndrome (GBS) following influenza vaccination. This work is ongoing and continues during each influenza season since its inception. OBE has conducted numerous epidemiological studies with private sector partners as well. In 2008, OBE began to work collaboratively with HealthCore to use population-based data to answer regulatory questions of public health importance for biologic products. This successful collaboration resulted in a number of peer-reviewed publications and contributed to FDA regulatory decision-making. In 2016, CBER funded a study using artificial intelligence, natural language processing and advanced analytics to evaluate biologic product adverse event reports to more efficiently analyze and review reported adverse events and trends in reports to support and enhance our postmarket safety surveillance work.
CBER is issuing this requirement, as part of its Biologics Effectiveness and Safety (BEST) initiative in its continuing efforts to develop new capabilities and build additional capacity for: 1) Blood safety surveillance as part of FDA’s efforts to build a national hemovigilance program; 2) New, innovative approaches to conduct postmarket safety and effectiveness studies for biologic products to include approaches and applications such as query tools, machine learning, artificial intelligence, natural language processing and others; and 3) Biologics effectiveness and safety surveillance efforts that may include vaccines, blood and blood products, tissues, and other biologic products. CBER’s BEST initiative expands our work beyond current partners, such as CMS and Sentinel, and may include work between CBER and some of the data, academic and other partners already engaged in these efforts. However, this request seeks to identify and develop new methods, approaches, and systems, possibly using new data sources, or common data models (CDM), and would not repeat work currently underway in those programs but is intended to expand CBER OBE’s safety and effectiveness work in the areas listed above. Access to large sources of patient data, especially inpatient data in Electronic Health Record format or access to claims data or inpatient claims data with access to medical charts is required. The proposed FDA work may be conducted under a number of possible organizational structures and arrangements. The data holder(s) or other organization(s) may have their own team of epidemiologists, subject matter experts, bioinformaticists, programmers and others who are experienced in conducting postmarket pharmacoepidemiological safety studies for drugs and biologics. Alternatively, the Contractor may work with an organization, such as a contract research organization or academic partner, which has its own team or may assemble its own team of such experts, which might serve as a Coordinating Center to manage the overall program work.

1.2 BIOLOGICS EFFECTIVENESS AND SAFETY (BEST) IDIQ OBJECTIVES AND SCOPE

The purpose of the Biologics Effectiveness and Safety (BEST) Contract is to conduct biologic product postmarket safety and effectiveness studies for products such as vaccines, blood, tissue and advanced therapeutic products regulated by CBER.

Objectives

The Contractor shall, independently and not as an agent of the Government provide all necessary personnel to assist in the development of capabilities for blood safety surveillance, postmarket safety and effectiveness studies for biologic products, and biologics safety surveillance efforts. Specifically, the primary objectives are to:

1. To provide the resources and support to establish a Coordinating Center that enables CBER to conduct active surveillance using a distributed data model
2. To develop new capabilities and build additional capacity in one or more of the following general areas including: 1) Blood safety surveillance in the postmarket setting as part of FDA’s efforts to build a national hemovigilance program; 2) New, innovative approaches to conduct postmarket safety and effectiveness studies for biologic products to include
approaches and applications such as query tools, machine learning, artificial intelligence, natural language processing and others; and 3) Biologics postmarket effectiveness and safety surveillance efforts that may include vaccines, tissues, and other biologic products.

3. Identify and use an appropriate data source(s) to conduct active biologic product postmarket safety and effectiveness studies by CBER using a distributed data model using a large data source.

Scope

The Contractor shall, independently and not as an agent of the Government provide all necessary personnel to assist in the development of capabilities for blood safety surveillance, postmarket safety and effectiveness studies for biologic products, and biologics safety surveillance efforts. Specifically, the primary objectives are to:

1. Establish a Coordinating Center with the resources such as relevant experts, methods and tools, access to large patient data sources to conduct biologic postmarket product safety and effectiveness assessments.
2. Provide a data source and distributed data model (with no direct FDA access to patient-identified data) and be able to access and analyze data using an approach such as a common data model (CDM), query tools and programs.
3. Provide capabilities to conduct rapid queries or simple safety studies using data, that include identifying patients with an exposure to the biologic product and outcomes of interest. For example, with respect to blood, exposure might include transfusion with whole blood, red blood cells, platelets, or other components. A health outcome of interest might include events such as transfusion-associated circulatory overload (TACO), hemolytic transfusion reactions (HTRs), and others to be determined on a task order basis by FDA) including ascertainment of incidence and prevalence rates.
4. Provide capabilities to conduct moderately complex query studies using cohort identification tools (control, treated populations, age stratification, and others) and evaluate unadjusted exposure. Ability to compare, correlate outcomes in different populations.
5. Provide capabilities to conduct highly complex epidemiological studies using a protocol that includes comparisons between cohort populations, and such methods as cohort designs, self-controlled risk intervals, and others. Contractor shall be able to validate coded exposure and outcome data using Medical Record Review (e.g., establish positive predictive value for the recorded health outcome of interest derived from electronic health records or claims data.
6. Provide or develop new, innovative approaches to conduct postmarket safety and effectiveness studies for biologic products or to conduct automated identification and reporting of blood and blood product adverse events to the FDA to include approaches and applications such as query tools, robotics, machine learning, artificial intelligence, natural language processing and others.
7. Conduct safety and/or effectiveness studies for biologics, such as blood and blood products, vaccines, and advanced therapy products.
8. Provide FDA staff training sessions on use of the methods and tools, data conducting queries and studies and Contractor resources developed to execute the indicated tasks to conduct postmarket safety and effectiveness studies.
2. TASK DESCRIPTION(S)

The following tasks constitute the performance of work expectations for BEST support.

2.1 TASK 1: PROGRAM AND TASK ORDER MANAGEMENT

The Contractor’s Program Manager and the Principal Investigator (PI) shall provide Program Management (PM) for the Biologics Effectiveness and Safety IDIQ requirements. These PM responsibilities shall include what is necessary to plan, structure, coordinate, schedule, manage, communicate, report, and steward all respective Task Orders and activities throughout the IDIQ’s period of performance.

As specified in the individual task order (ITO), the Contractor shall ensure smooth operations between its Coordinating Center, Data source(s) / partners, and work collaboratively with the FDA to ensure delivery of coordination activities such as kick-off meetings, bi-monthly telecons, monthly reports, and in-person meetings; and identify projects, develop protocols, reviewing deliverables such as protocols, interim analyses, interim reports and final reports.

The Contractor shall:

• Develop a plan on processes and procedures for collaborating with FDA in study design and analysis. Details of the collaboration will be determined on a task order basis, by mutual decision of all collaborative parties. Collaboration includes sharing summary data findings, interpretation of findings, review of manuscripts, design of protocols, and co-authorship of publications. The order of listing authors on each publication shall be determined on a case-by-case basis, by mutual decision of all collaborative parties and shall reflect appropriately each author's contribution to the project. Where there is no agreement on the above items, the FDA COR shall provide the final decision.
• Have the ability to contact a sample of physicians and/or patients on an ad hoc basis for information beyond what is available in automated data sources
• Generate a document providing information as to which key personnel will be used on each project and the percentage of time and staff member effort and contribution to the program on a per-task order basis.

Additionally, the Contractor shall provide both IDIQ-level Program Management services and Task Order-level Project Management services to establish control, management, monitoring, and notification mechanisms for Biologics Effectiveness and Safety System IDIQ requirement. Moreover, the Contractor shall work with the Government Contracting Officer (CO), Contracting Officer’s Representative (COR), and subject matter experts (SMEs) to ensure that tasks stay on track and important milestones are met.

Representative activities include, but are not limited to:

• Administering the IDIQ;
• Throughout the period of performance, developing, maintaining, modifying, and updating plans to include: task order (TO) risk management plans, staffing plan, Standard Operating Procedures (SOP), Protocols, and Others;
• For each TO, preparing a Task Order Management Plan (TOMP) describing the technical approach, organizational resources and management controls throughout TO execution.
• Preparing and maintaining the Program Management Plan;
• Preparing monthly progress and financial reports;
• Establishing notification mechanisms for acceptance by the FDA;
• Complying with reporting requirements;
• Following escalation procedures for problems, issues, and recommendations, as encountered;
• Safeguarding information;
• Managing Contractor staff and provide sub-contractor management;
• Coordinating tasks and working collaboratively with FDA CBER staff to carry out the work of the contract;
• Attending one annual face-to-face meeting with FDA CBER staff at the FDA White Oak Campus;
• Communicating, presenting and publishing of any Biologics Effectiveness and Safety project findings shall be done in coordination and with the concurrence of FDA CBER and the FDA COR;
• Ensuring proper exit criteria are followed when Contractor employees leave projects;
• Providing risk mitigation;
• Conducting and participating in progress meetings, facility meetings, training meetings, performance meetings, program/project reviews, management briefings, stakeholder presentations, demonstration meetings, transition meetings, and COR site visits, and post requirements meetings as may be required for each individual task order; and,
• Responding to ad hoc data calls to refine or confirm project findings or address FDA questions or concerns concerning project findings
• Provide training to FDA staff on data sources, study approaches or methods and tools employed and developed as part of the specific Task Orders and tasks. The specific type of training shall be determined based on the tools and methods developed and may include development of training manuals, conduct of training sessions, provide presentations or provide other similar activities.

2.1.1 TASK ORDER MANAGEMENT PLAN
As tasked, for each task order released under this IDIQ, the Contractor shall deliver a Task Order (TO) Management Plan. The TO Management Plan (TOMP) shall include a Work Breakdown Structure (WBS), which shall contain all of the work elements described in the IDIQ Task Order. The WBS elements shall also illustrate the sequence and resources required for each work package.

Additionally, the TOMP shall include a schedule that details activities, dependencies and timeframes for meeting FDA objectives and deliverables; an organizational chart identifying relationships, authorities, and responsibilities. The TOMP shall include a description of the management controls that the Contractor shall employ to meet the performance, cost, and schedule requirements; and other areas the Contractor deems relevant and important to the management of the Task Order. The Contractor shall ensure that activities are coordinated across task orders, if applicable, to promote cohesiveness among contracted activities.

The TOMP shall address all the action items from any Kickoff Meetings and other follow-on meetings, as appropriate. The Contactor shall update the TOMP when re-planning any activities. Changes to the
TOMP are subject to approval of the COR.

2.1.2 **MONTHLY STATUS REPORTS (MSRs)**

The Contractor shall provide a written Monthly Report (MSR) to the FDA IDIQ COR, incorporating all tasks at a high level and their progress. Within the first 30 calendar days after IDIQ award, the Government and the Contractor shall design and agree upon a standard reporting format and timeframe. At a minimum, unless otherwise specified in the individual Task Order (ITO), each MSR shall contain the following information:

- The previous month’s progress
- Deviance from previous month’s planned progress (either positive or negative)
- The current month’s planned progress
- Issues and recommendations
- Performance and Cost Report (P&CR): the P&CR shall include all recurring and non-recurring costs, cumulative cost, total labor hours, and cumulative labor hours for each task area for the previous month
- Program risks, risk mitigation plans, risk mitigation actions taken and resolution of risks.
- Status of deliverables

2.1.3 **KICKOFF MEETING**

Following the contract award, the Contractor shall conduct a kickoff meeting at the FDA for the BEST IDIQ. The kickoff meeting shall be conducted to introduce the Contractor team, discuss roles, responsibilities, the task order objectives, and other relevant issues.

2.1.4 **ANNUAL IN-PERSON MEETING**

The Contractor shall schedule and conduct an annual in-person meeting with FDA personnel at the FDA White Oak Campus in Silver Spring, MD to discuss Contractor’s performance under the contract; and provide a presentation of recently completed or in progress individual task order collaborative study or studies.

2.1.5 **TASK ORDER WORKGROUP MEETINGS**

The Contractor shall work collaboratively with FDA Staff and the COR and shall establish project workgroups and participate in bi-monthly telecons. The Contractor shall participate in the processes and meetings that support the overall efforts of the FDA Biologics Effectiveness and Safety System program and the work on each Task Order, including general Task Order management-related meetings, and meetings related to specific task areas. Generally, there are meetings of the Contractor and FDA Staff working group meetings on an approximately bi-monthly basis. The Contractor shall participate in different capacities, such as leading discussions; contributing questions and answers; raising issues, risks and concerns; and developing and giving presentations. Meeting information shall be stored in the appropriate Contractor document repository and accessible to FDA staff. The Contractor shall prepare and track meeting agendas, minutes, issues, risks, and action items as requested by FDA. Minutes shall be of sufficient detail to accurately document meeting date and location, meeting purpose, items
discussed, decisions made, attendees, and action items, and shall be delivered within FDA document repositories.

2.1.6 RISK MANAGEMENT
The Contractor shall identify and report for resolution to the Government any issues that prevent the Contractor from performing the work in any Task Order that the Contractor is unable to resolve independently. For each Task Order, the Contractor shall document and report the risks and opportunities within a risk registry. The Contractor shall maintain the risk registry and provide it to the COR on request.

The risk registry shall contain, at a minimum, unless otherwise specified in the ITOs:
- Issue Number: a sequential numbering of all issues;
- Severity: assessment of issue severity i.e., likelihood and consequences (High/Medium/Low);
- Date Found: – date that issue was identified by the Contractor;
- Duration: number of days that issue has been open;
- Status: representing issue status as open or closed. The Contractor shall maintain a complete list of all issues – no issues typically should be deleted from the Contractor’s delivered list;
- Title: short description of issue;
- Updated: date for updated status;
- Details: narrative description of activities that have been completed to resolve issue;
- Assigned To: identify Government POC or Contractor that is assigned to resolve the issue;
- Solution or Workaround: description of the actions and activities taken to resolve or mitigate issue the issue.

2.1.7 FACILITIES
The Contractor shall provide all facilities and equipment necessary to conduct the proposed safety and effectiveness work, in order to accomplish the IDIQ requirements as specified herein. Additionally the Contractor shall ensure that electronic data and medical record data is securely stored, transferred and handled, and retained and protected for future study purposes.

2.1.8 DELIVERY INSTRUCTIONS FOR DELIVERABLES
Unless otherwise specified, all deliverables, reports or copies of reports shall be delivered to the COR. Requirements for inspection and acceptance are as follows:

- The COR or the POC designated in each TO, will inspect and accept the services provided to ensure they meet the requirements detailed in the relevant IDIQ task order.
- The Government will accept products and services only if they conform to all terms and conditions of the IDIQ and each TO.
- The Government will provide written notification of acceptance or rejection within ten (10) calendar days of receiving the service.
- The Government will reject non-conforming products and services. The Contractor shall correct any deficiencies within thirty (30) calendar days of when the Government issues the rejection.
notice. If the Contractor cannot correct the deficiencies within this time frame, the Contractor shall immediately notify the COR of the reason for the delay and provide a proposed corrective action plan within ten (10) calendar days.

In addition, the Contractor shall be proactive in informing the designated CBER COR of any issues, problems and recommendations that shall be addressed in order for the overall effective accomplishment of contract goals and deliverables. Recommendations for actions that need to be taken by FDA staff, or other Contractors shall be clearly defined and communicated (via email) to the responsible party and the FDA, and have identified dates for completion.

2.2. **Task 2: Transition Services**
Transition activities take place to efficiently transition all activities from the incumbent Contractor to the new IDIQ Contractor. Currently, there is no incumbent Contractor since this is a new contract. As tasked, the Contractor may be required to develop transition-out plans and conduct transition activities for task orders issued against this IDIQ vehicle.

2.2.1 **Transition-Out**
The Contractor shall facilitate the transition-out of contracted activities and services to the Federal Government or, to a follow-on Contractor by the end of the contract period of performance.

The Contractor shall provide support for transition-out activities. During this period, the Contractor shall ensure no degradation in support provided under the task order. Between the turnover date designated by the COR and the end of the contract period of performance, the outgoing Contractor shall ensure all task order activities are closed out and provide sustainment support to complete the transition.

Representative deliverables include, but are not limited to:

- Developing and submitting a Transition-Out Plan and Schedule to the COR
- Providing the FDA with current versions of all documentation developed (i.e. Standard Operating Procedures and Manual of Operations)
- Providing the FDA with a current inventory of all Government-Furnished Equipment (GFE) and Government Furnished Information (GFI) utilized by the Contractor along with full support in the reconciliation of this inventory
- Providing the follow-on contractor with the ability to “shadow” and participate in technical exchange meetings and opportunities to facilitate the transfer of information, processes, and data needed to continue the services being performed by the Contractor

2.3 **Task 3: Establish Organization and Infrastructure**

The primary goal of this Contract is to gain access to methods and tools, infrastructure and data resources a to conduct epidemiologic safety studies that promote OBE’s mission to assure the safety and effectiveness of biologic products including vaccines, blood, tissues and advanced therapeutic products. This Contract builds and expands upon activities undertaken as part of previous FDA collaborative studies for biologic product safety.
During the course of the contract period of performance, the Contractor shall provide a work plan(s) and a cost estimate(s) for each specific biologic safety study requested. The Contractor shall not proceed with the work plan until written approval is given by both the Contracting Officer and COR. The following describe in greater detail Contractor activities for each of the objectives of the Contract.

General Requirements: Please note that the requirements below refer to all biologic products, including vaccines, blood and tissue products.

Data Organization and Resource Requirements. The Contractor shall:

- Establish a Coordination Center (CC) or similar organizational structure consisting of a team of experts such as epidemiologists, clinical and subject matter experts, bioinformaticists, programmers, project managers and others.
- Be capable of executing the work of the TOs including but not limited to identifying the data necessary to conduct the work; develop the study protocols and programming and conducting the required development of methods or tools and/or postmarket pharmacoepidemiological analyses and safety studies for biologics.
- Collaborate with FDA by providing US health encounter data for pharmacoepidemiologic studies. The Contractor shall provide documentation that the Contractor either owns the data or has legal rights to access and disclose analyses of the data to third parties such as the FDA.
- Provide a data resource that can best support population-based studies of blood or blood product, vaccine, or other biologic product safety and effectiveness and is automated with a computerized system available for linking each patient to all relevant medical care data including enrollment status, biologic product exposure data, coded medical outcomes, and vital records (desired, but not required). For biologics licensed for distribution in the US see http://www.fda.gov/CBER/products.htm and for vaccines see http://www.fda.gov/CBER/vaccine/licvacc.htm.
- Provide a document with database detail (further defined at the TO level) so that FDA has the ability to estimate the contribution of various risk factors associated with the occurrence of medical events of interest, including product lot identities if possible.
- Provide a document detailing the ability to form groups (i.e., cohorts) of patients exposed to one or more biologic products and to follow them for the occurrence of one or more medical outcomes.
- Provide a document demonstrating full disclosure of HIPAA-compliant data collection, coding, and configuration methods to allow FDA to appropriately interpret findings.
- Summarize the data for FDA use. FDA will require no patient-, provider-, or health plan-specific identifiers. The de-identification of the data shall be solely the responsibility of the Contractor.
- Deliver a document confirming automated data through chart review and/or other reliable and valid means.

Representative deliverables include, but are not limited to:

- Coordinating Center
- Provide Data resource to support population-based epidemiological studies of safety and effectiveness
• Provide Document providing sufficient database detail so that FDA can estimate its ability to meet criteria for doing the proposed studies, ability to be analyzed by tools, ability to identify cohorts and study groups, etc.
• Document demonstrating HIPAA-compliant data collection, coding and configuration methods
• Document ability to confirm data and validate coding through medical chart review

2.4. TASK 4: ESTABLISH BIOLOGICS EFFECTIVENESS AND SAFETY SYSTEM PROTOCOLS AND PROCEDURES

The Contractor shall work collaboratively with the FDA to develop and finalize the Biologics Effectiveness and Safety System project protocols and manual of operating procedures (MOP), and update as needed to reflect the ITO activities. The Contractor shall obtain and meet all required review, approval and standards processes that comply with all relevant institutional, federal, state, and local laws and regulations to conduct the work such as Institutional Review Boards (IRB), data and information technology security, such as Federal Information Security management Act (FISMA), Health Insurance Portability and Accountability Act (HIPAA) and any others identified in the ITO. These procedures (i.e. the MOP) shall address at a minimum the following: data collection, handling, sharing, ownership, and security; management and tracking, consensus definitions, transfer, and sharing considerations for data summaries.

Representative activities include, but are not limited to:
• Developing and implementing secure and robust data collection, data quality control, tracking, management, and storage procedures for data, each analysis and for all analyses.
• Developing a query intake form or protocol for large complex analyses. Each document shall provide the stated regulatory question to be addressed, Indicate data to be used, including years, protocols shall include a draft feasibility analysis and power calculations for sample size, estimated numbers of patients/patient records, cohorts to be studied including control and treatment populations; methods used and rationale;

Representative deliverables specific to the ITO include, but are not limited to:
• Biologics Effectiveness and Safety Project Protocols
• A new tool or method for conducting automated safety reporting that has been quality control checked and validated
• Query report, including completed form, description of analyses and summary tables and findings
• Interim reports summarizing pilot, preliminary or near final findings.
• Final Report for protocol-based studies providing findings in tabular format, detailed summary of findings, discussions of strengths, limitations and other related aspects of importance.
• For innovative methods and tools such as AI, machine learning, NLP and others: provide a final report describing overall approach used including tools, methods, data sources, etc. along with a description of strengths, challenges and limitations of automation process.

2.5. TASK 5: BIOLOGIC PRODUCT-SPECIFIC TOOLS, DATA AND RESOURCE REQUIREMENTS
The Contractor shall:

- Identify potential tools and methods that could best support population-based studies of biologic product safety. The ability of the tools to query data sources for evaluating safety and effectiveness of FDA-regulated biologics (including blood and blood products, human tissues, vaccines, vaccines, and advanced therapy products).
- For each method and tool, provide a detailed description of scientific underpinnings, experience with use of each, and any validation information of tool performance to evaluate safety and effectiveness of drugs or biologics using large patient data sources.
- Identify potential data source(s) that could best support population-based studies of biologic product safety. The ability of the data source(s) to capture FDA-regulated biologics (including blood and blood products, human tissues, vaccines, vaccines, and advanced therapy products) should be evaluated.
- Provide exposure data on selected approved biologic products.
- Provide data and preliminary analyses (including numbers of patients utilizing a specific biologic product, their age and gender, and crude counts of outcomes) to determine the feasibility of formal studies within 4-6 weeks of data request.
- For each potential data source and/or data environment, describe the types of electronic healthcare data (e.g., claims/transactional, laboratory, blood or blood product, vaccine or biologics inventory or tracking systems, pharmacy, medical records, other) that could be used to identify product usage and subsequent healthcare claims. Description of each data type should include (but not be limited to):
  - Structure and coding, including consistency with widely recognized standards;
  - Completeness, timeliness, and accessibility of data, including estimated times from service delivery to accessibility of data via queries;
  - Level of detail available to examine type, frequency and dose number of vaccine or biologic product administered;
    - Assess ability to identify biologic products by type, lot identification number, or other applicable descriptors.
  - Level of detail available to examine temporal relationships between vaccine or biologic product administration and associated adverse events/outcomes. Examples of products and adverse event associations of interest include, but are not limited to:
    - Anaphylaxis after vaccination, immune globulin intravenous (IGIV) and other plasma derivatives, and other biologics by age group.
    - *Idiopathic thrombocytopenic purpura* (ITP) after vaccination with live virus vaccines, including influenza, and after trivalent inactivated influenza vaccines by age and vaccine dose;
    - Transverse myelitis (TM) after vaccination.
    - Guillan-Barre Syndrome (GBS) after influenza vaccination.
  - Assess ability to identify transfused blood components by type, number of transfused units, unit identification number, or other applicable descriptors.
Assess ability to identify use of human tissues by tissue type (e.g. bone, skin, musculoskeletal soft tissue), source (e.g., allograft, autograft) and surgical procedure.

Specific product and adverse event associations for study will be further developed in collaboration with FDA during TO process.

Special informational considerations for biologic product safety, including the data source's ability to:

- Link product administration/treatment records with inpatient and outpatient data including emergency department treatment.
  - Identify the dose number, and lot information.
  - Identify the time interval in hours, when necessary, between vaccination or product administration and onset of adverse events.
- Accurate identification of adverse event onset time.
- Identify prior vaccination or treatment and medical history.

Potential limitation if used for post-market product safety surveillance.

Description of pharmacy data should include (but not be limited to) availability of data for: prescribing-only v. transactional/claims v. documentation of actual product use/administration, new molecular entities, brand-name v. generic products, dosing, route of administration. Description of medical data on diagnoses, procedures, and laboratory values should include a description of the coding systems used (Common Data Interchange Standards Consortium (CDISC) and Logical Observation Identifiers Names and Codes (LOINC) preferred).

- For each potential data source/and or environment, describe the patient population, participating institutions, and patient care settings.
  - Description of patient populations should include (but not be limited to): payor status (if applicable), criteria for inclusion/exclusion, average length of follow-up, loss to follow-up, and participation in other healthcare systems.
  - Description of the patient populations' representativeness should include (but not be limited to) comparisons of its size and patient characteristics to the respective catchment area(s) and national-level data.
  - Description of patient care settings should include (but not be limited to): number, types, and catchment areas of participating institutions; estimated annual number of patients and/or visits in each setting; ability to longitudinally track patients through different settings, including content and quality of data available in each setting.
  - Estimate the proportion of the total population with clinical/medical data available (i.e., enrolled patients) that receives biologic products on an annual basis, and the average annual loss of enrollees among this group.
  - Identify the proportion of product utilizations occurring in each patient care setting, including, if available, outpatient settings, inpatient settings, and others.
For each potential method, tool and data source/environment, describe experience and feasibility to evaluate biologic product safety.

- Describe ability and expertise in developing medical diagnostic/procedure coding or other criteria to identify utilization of specific blood, vaccine or biologic products.
- Describe ability and expertise in developing clinically relevant medical diagnostic coding or other criteria to identify adverse events of interest.
- Assess the data source's ability to identify and select clinically comparable control groups for studying healthcare outcomes.
- Assess ability to validate exposure and outcome data through medical record review, use of established, validated medical coding lists or other methods.
- Assess the ability to extrapolate both the utilization and patient-level data to national estimates of biologic product utilization and adverse event patterns in the U.S. The methods for sampling and projection to national estimates shall be valid, reliable, and robust, and the methods fully disclosed.

Specific biologic product and adverse event associations, and appropriate comparison groups, for study will be further developed in collaboration with FDA during the TO process.

- For each potential data source and/or environment, describe prior and current uses of biologic product data, including (but not limited to): post-market safety surveillance, administrative purposes, quality assessment/improvement and/or benchmarking, academic/industry research. This should include (but not be limited to):
  - Representative examples of publications and/or presentations related to biologic product safety that have been developed using these data;
  - Letters of support and curriculum vitae from internal and external users/researchers that describe:
    - Their experience and knowledge in working with the data source and/or environment;
    - Strengths and potential limitations of working with data source and/or environment for post-market surveillance;
    - Each reference's current and prior relationships (financial or otherwise) with this and other potential data sources;
    - Plans for future data source enhancements.

3. **CONTRACT CONSTRAINTS**

The following constraints are applicable to this contract:

1. The Contractor shall ensure that all appropriate administrative and regulatory approvals are obtained. These include but are not limited to those that address human subject considerations; and clearances including applicable Institutional Review Boards (IRBs), and Office of Management and Budget (OMB) which will be detailed during the ITO process.

2. Interim data used in technical progress reports and other reports developed for the purpose of study monitoring and shall not be released publicly. Premature release of such data could result in interpretations that prove to be unreliable or invalid once the study is completed and the full
context for the data is known and lead the public and medical practitioners to pursue inappropriate measures.

3. The Contractor shall be responsible for knowledge of and compliance with all applicable federal information technology and information management laws, regulations, policies and standards at the government-wide, HHS and FDA levels.
   i. The computer programs, data management systems, databases, and other resources used or developed through this contract shall comply with data standards and procedures established by DHHS and FDA (per http://www.fda.gov/ForIndustry/DataStandards/default.htm).

4. The Contractor shall not use confidential or otherwise privileged information shared by FDA with contractors to solicit or in any way encourage industry funding/financial sponsorship of research projects to be performed by the contractor. In the event that a third party, such as a drug sponsor, independently requests that the contractor conduct research on a safety issue the contractor may conduct such research only if both of the following conditions are satisfied: (1) the contractor shall not divulge confidential and privileged information previously shared by the FDA; and (2) the contractor shall recuse itself from all subsequent conversations with FDA about the safety of the involved biologic product(s). In conjunction with the above, the contractor shall provide a Conflict of Interest Plan as outlined in FDA Clause 1337 Conflict of interest (see FDA 1337, Conflict of Interest).

5. The Contractor shall work collaboratively with FDA CBER during the task order proposal request, projects will be mutually agreed upon by both parties and final approval is required by the FDA COR. Communications, presentations, and publications require internal FDA clearance of up to 30 days. Generally, the FDA COR will offer final decision on products and FDA CO approval will be needed on any modifications to the contract or ITOs.

4. OTHER REQUIREMENTS

4.1 KEY PERSONNEL
Per HSSAR 352.237-75, the key personnel specified in this IDIQ are considered to be essential to work performance. At least 30 days prior to diverting any of the specified individuals to other programs or contracts (or as soon as possible, if an individual must be replaced, for example, as a result of leaving the employ of the Contractor), the Contractor shall notify the Contracting Officer. The Contractor shall submit a comprehensive justification for the diversion or replacement request (including proposed substitutions for key personnel) to permit evaluation by the Government of the impact on performance under this Contract. The Contractor shall not divert or otherwise replace any key personnel without the written consent of the Contracting Officer.

Key Personnel at the IDIQ-Level are:
- Principal Investigator
- Program Manager

Key Personnel may be assigned at the ITO level also.
4.2 **Government Furnished Information (GFI) / Government Furnished Equipment (GFE)**

The FDA does not intend to provide the Contractor with any Government Furnished Information (GFI) or Government Furnished Equipment during the period of performance of this contract. The FDA will specify any GFI and GFE requirements in future individual task orders (ITOs).

4.3 **Travel**

Performance under this IDIQ may require contractor employees to travel. If travel within the continental United States (CONUS), is required, the contractor is responsible for making all needed arrangements for its employees.

The Government will not reimburse the contractor for local travel costs incurred within the Washington DC (50-mile radius). All travel shall be in accordance with rules set forth for temporary duty travel in FAR 31.205-46 and the Federal Travel Regulation (http://www.gsa.gov/portal/content/102886). Travel and Per Diem authorized reimbursed under this contract shall not exceed the Government approved rates in effect (https://www.gsa.gov/portal/content/104877).

The contractor shall submit all travel requests to the COR and the Contract Officer for review and approval at least 10-calendar days in advance.

4.4 **IDIQ Administration**

4.4.1 **Period of Performance**

The period of performance for this IDIQ vehicle will have a five (5) year ordering period. Individual tasks orders awarded under this IDIQ contract shall be for periods of varying duration, but are anticipated to range from 12- to 60-months.

4.4.2 **Place of Performance**

The Contractor shall perform specified duties at its own site or contractor shall indicate in the ITO proposal if there is a necessity for some staff to work on-site at the FDA.

4.4.3 **Government Points of Contact (POCS)**

IDIQ Contract Officer Representative (COR):

To be identified at award