

FDABAA-15-00121**Overview Information**

Agency Name: Department of Health and Human Services, Food and Drug Administration, 10903 New Hampshire Avenue, Silver Spring, Maryland, 20993

Issuing Office: Department of Health and Human Services, Food and Drug Administration, Office of Acquisitions & Grants Service, 5630 Fishers Lane, Rockville, MD 20857

Research Opportunity Title: Food and Drug Administration Broad Agency Announcement for the Advanced Research and Development of Regulatory Science

Announcement Type: Broad Agency Announcement

Eligible Applicants: This BAA is open to **ALL** responsible sources. Offerors may include single entities or teams from private sector organizations, Federally Funded Research and Development Centers (FFRDCs) (see page 4 for FFRDC eligibility requirements) and academic institutions.

Research Opportunity Description: Food and Drug Administration solicits the advanced research and development for regulatory science. FDA anticipates that research and development activities awarded under this BAA will serve to advance scientific knowledge to accomplish its mission to protect and promote the health of our nation.

Types of instruments that may be awarded: Procurement Contracts

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FDA BAA-15-00121

INTRODUCTION

Advancing Regulatory Science and Innovation

This Broad Agency Announcement (BAA), which sets forth research areas of interest for Food and Drug Administration is issued under FAR 35.016(c) of the Federal Acquisition Regulation (FAR). The purpose of this BAA is to fulfill an FDA requirement to utilize industry capabilities to advance the state of the art and achieve improvements in technology, materials, processes, methods, devices, or techniques in specific topics as described in this document. Proposals selected for award are considered to be the result of full and open competition and in full compliance with the provision of Public Law 98-369, "The Competition in Contracting Act of 1984" and subsequent amendments.

The Food and Drug Administration (FDA) protects and promotes the health and safety of all Americans through enhancing the availability of safe medical products and foods and promoting innovation that addresses unmet medical and public health needs. FDA also protects and promotes the health and safety of animals through assuring the availability of safe animal drug products and food. FDA is a science-based regulatory agency and a critical component to the success of the nation's public health, health care systems, and economy. FDA was created in 1906 as one of our nation's principal consumer product protection agencies, and is now responsible for assuring the safety of biologics, such as blood products and vaccines, drugs, medical devices, foods, cosmetics, and many other consumer goods. Since 2009, it has also been responsible for regulating the manufacture, marketing, and distribution of tobacco products.

In the US, FDA-regulated products account for about 25 cents of every dollar spent by American consumers each year — products that touch the lives of every American every day. FDA is responsible for advancing the public health by helping to speed innovations that make foods safer and make medicines and devices safer and more effective. At the same time, FDA helps consumers and health care providers get the accurate and science-based information they need to make the best possible decisions about their use of medical products and foods for human and non-human animal use. FDA must make decisions based on the best available scientific data and using the best tools and methods available in order to ensure products meet the highest quality standards for consumers, while at the same time fostering and advancing innovation in the products it regulates.

The core responsibility of FDA is to protect consumers by applying the best possible science to its regulatory activities — from pre-market review of efficacy and safety to post-market product surveillance to review of product quality. In the last few years, rapid advances in innovative science have provided new technologies to discover, manufacture and assess novel medical products, and to improve food safety and quality; FDA must keep pace with and utilize these new scientific advances to accomplish its mission to protect and promote the health of our nation.

The BAA is open to all responsible sources. Offerors may include single entities or teams from private sector organizations, Federally Funded Research and Development Centers (FFRDCs), and academic institutions. Non-U.S. organizations and/or individuals may participate to the extent that such participants comply with any necessary nondisclosure agreements, security regulations, export control laws, and other governing statutes applicable under the

circumstances.

Federally Funded Research and Development Centers (FFRDCs) and Government entities (e.g., Government/National laboratories, military educational institutions, etc.) are subject to applicable direct competition limitations and cannot propose to this BAA in any capacity unless they meet the following conditions:

1. Clearly demonstrate that the proposed work is not otherwise available from the private sector.
2. Provide a letter on official letterhead from their sponsoring organization citing the specific authority establishing their eligibility to propose to Government solicitations and compete with industry, and their compliance with the associated sponsoring agreement and terms and conditions.

Historically Black Colleges and Universities (HBCU), Minority Institutions (MI), Small Business concerns, Small Disadvantaged Business concerns, Women-Owned Small Business concerns, Veteran-Owned Small Business concerns, Service-Disabled Veteran-Owned Small Business concerns, and HUB Zone Small Business concerns are encouraged to submit proposals and to join other entities as team members in submitting proposals.

The purpose of this BAA is to solicit proposals that focus on one or more of the following areas of interest as listed here and further described in Part I of this announcement.

1. Modernize Toxicology to Enhance Product Safety
2. Stimulate Innovation in Clinical Evaluations and Personalized Medicine to Improve Product Development and Patient Outcomes
3. Support New Approaches to Improve Product Manufacturing and Quality
4. Ensure FDA Readiness to Evaluate Innovative Emerging Technologies
5. Harness Diverse Data through Information Sciences to Improve Health Outcomes
6. Implement a New Prevention-Focused Food Safety System to Protect Public Health
7. Facilitate Development of Medical Countermeasures to Protect Against Threats to U.S. and Global Health and Security
8. Strengthening Social and Behavioral Science at FDA by Enhancing Audience Understanding
9. Strengthening the Global Product Safety Net

Multiple awards are anticipated. The amount of resources made available under this BAA will depend on the quality of the proposals received and the availability of funds. Anticipated funding for the program (not per contract or award) may range from \$200,000 to \$50,000,000 dollars subject to congressional appropriations. This funding profile is an estimate only and will not be a contractual obligation for funding. All funding is subject to change due to government discretion and availability.

The Government reserves the right to select for negotiation all, some, one, or none of the proposals received in response to this solicitation, and to make awards without discussions with proposers. The Government also reserves the right to conduct discussions if it is later determined to be necessary. If warranted, portions of resulting awards may be segregated into pre-priced options. Additionally, FDA reserves the right to accept proposals in their entirety or to select only portions of proposals for award. In the event that FDA desires to award only portions of a proposal, negotiations may be opened with that proposer. The Government reserves the right to fund proposals in phases with options for continued work at the end of one or more of the phases.

To be eligible for award, a prospective recipient must meet certain minimum standards pertaining to financial resources, ability to comply with the performance schedule, prior record of performance, integrity, organization, experience, operational controls, technical controls, technical skills, facilities, and equipment.

This BAA is available on the following websites:

<https://www.fbo.gov>

<https://www.fda.gov>

This BAA is a continuously open announcement valid throughout the period from the date of issuance through the closing date specified in fbo.gov. Amendments to this BAA will be posted to fbo.gov when they occur. Interested parties are encouraged to periodically check these websites for updates and amendments.

Part I: Research Areas of Interest

Through this BAA, FDA seeks to support advanced research and development strategies in the following research areas of interest. This section presents the technical objectives that FDA seeks to achieve through this BAA. Offeror's shall propose a Statement of Work (SOW) that is consistent with research and development work as defined in FAR 35.001. Proposal preparation and submission instructions are contained in Part III.

1. Modernize Toxicology to Enhance Product Safety

FDA seeks to improve the prediction of product safety and efficacy based on preclinical data by conducting internal and collaborative research and development. Areas of interest include:

1.1 Develop better models of human adverse response:

- 1.1.1 Evaluate and promote the use of cell and tissue based assays that more accurately represent human susceptibility than animal models to adverse reactions;
- 1.1.2 Modernize the development and use of animal models that consider the potential influence of disease progression and disease co-morbidities on the emergence of adverse events;
- 1.1.3 Promote a better understanding of toxicity mechanisms by evaluating safety assessment data at multiple levels of biological organization including genes, proteins, pathways, and cell/organ function;
- 1.1.4 Assess and characterize molecular targets and host genetic factors that may be associated with rare and unexpected adverse events ("off-target" drug effects);
- 1.1.5 Initiate *in vitro* and *in vivo* studies to identify potential markers of harm associated with exposure to tobacco constituents; and
- 1.1.6 Initiate *in vitro* studies to identify potential markers of harm associated with exposure to medical products.

1.2 Identify and evaluate biomarkers and endpoints that can be used in non-clinical and clinical evaluations:

- 1.2.1 Evaluate the accuracy (specificity and sensitivity) with which animal models and *in vitro* assays correctly predict potential human risk;
- 1.2.2 Assess concordance between animal and human markers of toxicity and determine how the performance of these markers and their interpretation may vary across different organ systems and human populations; and
- 1.2.3 Evaluate quantitative imaging (e.g. positron emission tomography, magnetic resonance imaging, computed tomography) and other advanced approaches (e.g. metabolomics) for identifying new biomarkers and predictors of efficacy and safety.

1.3 Use and develop computational methods and in silico modeling:

- 1.3.1 Improve the use of chemical Structure-Activity Relationship (SAR) models in the prediction of human risk and integrate this analysis into the review process;
- 1.3.2 Develop and implement approaches to link chemical structures and substructures to a wide range of information about product safety, disease targets, and toxicity mechanisms;
- 1.3.3 Develop clinical trial simulation models that can reveal interactions between drug or device effects, patient characteristics, and disease variables influencing outcomes;
- 1.3.4 Develop computer models of cells, organs, and systems to better predict product safety and efficacy;
- 1.3.5 Develop computer models that integrate pharmacokinetic, pharmacodynamic, materials science, or mechanistic safety data to predict clinical risk-benefit and confirm post-marketing safety in different patient populations; and
- 1.3.6 Develop and apply data mining, knowledge building, and data visualization tools to inform computer model development, clinical risk prediction, and regulatory decision-making.
- 1.3.7 Develop computer models for assessing the risk of new tobacco products that will potentially enter the market by considering potential risks to users of the products based on demographic attributes of the users and usage patterns.

1.4 Develop Better Models to Investigate the Toxicology of Veterinary Drugs

- 1.4.1 Assesses whether zebrafish (*Danio Rerio*) serve as a good model to investigate the potential toxicity or health effects of approved and unapproved animal drugs.

2. Stimulate Innovation in Clinical Evaluations and Personalized Medicine to Improve Product Development and Patient Outcomes

FDA seeks to develop new tools and approaches needed to catalyze the development of personalized medicine and to modernize and advance the science and conduct of clinical trials. Areas of interest include:

2.1 Develop and refine clinical trial designs, endpoints and analysis methods:

- 2.1.1. Refine clinical trial design and statistical methods of analysis to address issues such as missing data, multiple endpoints, patient enrichment, and adaptive designs;
- 2.1.2 Identify and evaluate improved clinical endpoints and related biomarkers for trials in areas where optimal endpoints are lacking (e.g., efficacy and safety endpoints for osteoarthritis in humans and animals, for gene therapy, for transplant-related studies (endpoints and duration), for ophthalmic indications, for tumor vaccines, and for stem cell-derived therapies);
- 2.1.3 Develop novel trial designs and endpoints for special needs (e.g., small trials for orphan indications, designs and endpoints for pediatric trials including neonatal trials);

- 2.1.4 Continue to refine the use of modeling and simulation in clinical trial design to enhance the effectiveness of clinical studies; and
- 2.1.5 Develop practical methods to assess the bioequivalence of locally acting drugs, including inhalants, topicals, and intraluminal GI drugs.

2.2 Leverage existing and future clinical trial data:

- 2.2.1 Develop quantitative models and measures of disease progression; and
- 2.2.2 Utilize large, pooled clinical trial datasets to identify potential trial endpoints, explore differences in specific populations and subpopulations (e.g., stage of disease, chronic disease states, sex, race and ethnicity, pediatrics and other age groups) and different subsets of diseases, improve understanding of relationships between clinical parameters and outcomes, and evaluate clinical utility of potential biomarkers.

2.3 Identify and qualify biomarkers and study endpoints:

- 2.3.1 Facilitate identification and qualification of new and improved biomarkers for safety and efficacy, pharmacodynamic response - dose selection, disease severity, progression and prognosis, and pharmacogenomics (to predict safety and efficacy or guide dosing); and
- 2.3.2 Develop and evaluate novel approaches for biomarker identification, including 'omics, systems biology, and high throughput methods.

3. Support New Approaches to Improve Product Manufacturing and Quality

FDA seeks to support the application of novel technologies to product development and innovative analytical approaches to improve product manufacturing and quality through active research. Areas of interest include:

3.1 Enable development and evaluation of novel and improved materials and manufacturing methods:

- 3.1.1 Investigate the effects of continuous manufacturing (manufacturing using a continuous process, rather than a batch approach) on product quality;
- 3.1.2 Examine specific novel material and manufacturing technologies to determine how they impact product failure rates; and
- 3.1.3 Evaluate the role excipient ingredients and complex dosage forms on product safety, efficacy, and quality and further two state-of-the-art manufacturing strategies-Process Analytical Technology, and Quality-By-Design approaches-for impact on manufacturers' ability to maintain consistent quality.
- 3.1.4 Explore novel approaches to incorporating medical device development concepts and methodologies, including quality and risk management.

3.2 Develop new analytical methods:

- 3.2.1 Investigate feasibility and value of using emerging and improved analytical technologies like NMR (Nuclear Magnetic Resonance), mass spectrometry, or near infrared or Raman spectroscopy for evaluating product quality of pharmaceutical agents, and evaluate whether these technologies should replace existing methods;
- 3.2.2 Evaluate applicability of various analytic technologies for determination of the “similarity” of biosimilars to their reference products;
- 3.2.3 Perform statistical research to support development and evaluation of new assays and tests needed to assure analytical methods give consistent reproducible results; and
- 3.2.4 Develop improved methods and tools to detect and measure the physical structure, chemical properties, and safety of engineered nanomaterials and complex dosage forms (e.g., transdermal patches, inhalation delivery systems, and targeted drug delivery systems etc.) in FDA-regulated products.
- 3.2.5 Develop Methods to Assess Quality of Glycerin

Develop methods to identify the quality (crude vs industrial vs usp) and potential contaminants in the various glycerin grades used in finished products (for example jerky pet treats for animals, drugs for humans and animals).

3.3 Reduce risk of microbial contamination of products:

- 3.3.1 Develop sensitive, rapid, high-throughput methods to detect, identify, and enumerate microbial and chemical contaminants and validate their utility in assessing product sterility; and
- 3.3.2 Develop and evaluate methods for microbial inactivation/removal from medical products that are not amenable to conventional methods of sterilization.

3.4 Improve scientific approaches to evaluate generic drugs

In July 2012, Congress passed the Generic Drug User Fee Amendments (Title III of the Food and Drug Administration Safety and Innovation Act (Public Law 112-144)). The Generic Drug User Fee Amendments (GDUFA) is designed to enhance public access to safe, high-quality generic drugs, and to reduce costs to industry. To support this goal, FDA agreed in the GDUFA commitment letter to consult with industry and the public in order to create an annual list of regulatory science initiatives specific to research on generic drugs for each year covered by GDUFA. The research activities related to the FY 2014 topic areas are as follows:

- 3.4.1 Post-market Evaluation of Generic Drugs
 - 3.4.1.1 Develop surveillance and monitoring methods for generic drugs.
 - 3.4.1.2 Understand patient perceptions of generic drug quality and effectiveness.
 - 3.4.1.3 Evaluate and verify therapeutic equivalence via brand to generic switching studies in patients for anti-epileptic drugs, immunosuppressant drugs, bupropion, ADHD

drugs and cardiovascular drugs.

3.4.2 Equivalence of Complex Products

Develop research studies to establish bioequivalence methods for complex products such as liposomes, sustained release parenterals, and complex mixtures.

3.4.3 Equivalence of Locally Acting Products

Develop research studies into new bioequivalence (BE) methods and pathways for local acting drugs for inhalation, topical dermatological, nasal, GI acting, ophthalmic and otic products.

3.4.4 Therapeutic Equivalence Evaluation and Standards

3.4.4.1 Develop risk-based equivalence standards for narrow therapeutic index (NTI) drugs.

3.4.4.2 Investigate patient use factors such as tablet size for their impact on generic substitutability.

3.4.4.3 Evaluate IVIVC/predictive dissolution for solid oral dosage forms.

3.4.5 Computational and Analytical Tools

3.4.5.1 Develop modeling and simulation tools including PBPK/absorption models, PD models/clinical trial simulation, and quantitative risk modeling for generic drugs.

3.4.5.2 Develop analytical methods to characterize peptides and other complex mixtures and particle size and surface chemistry for potential generic products.

3.5 Identify and Qualify Pain-Associated Biomarkers that are Associated with Therapeutic Control of Pain in Food Producing Animals

3.5.1 Identify molecular biomarkers (proteomic or genomic) that can be qualified against clinical signs to serve as surrogate endpoints in assessing the capacity of therapeutic agents to alleviate pain in food animals such as cattle, pigs, and goats.

3.6 Develop a Regulatory Database for Species Identification

3.6.1 Develop a DNA barcode sequence database for species identification

4. Ensure FDA Readiness to Evaluate Innovative Emerging Technologies

FDA seeks to evaluate new and emerging technologies through active research intramurally and collaboratively with external partners. Areas of interest include:

4.1 Develop assessment tools for novel therapies:

4.1.1 Develop new approaches such as *in vitro* and *in vivo* methods to identify measurable characteristics of product safety, quality, and potency when evaluating new therapeutics (e.g., engineered tissues or cell therapy products, including stem cell-derived products, for

clinical application in regenerative medicine, additive manufacturing in medical products, nanotechnology in medical products);

- 4.1.2 Develop new ways to evaluate gene therapy and antisense therapy products developed in this period of fast-paced scientific progress;
- 4.1.3 Integrate an understanding of product quality and safety based on novel genomic, proteomic, metabolomic, and other -omic technologies; and
- 4.1.4 Explore the role of wireless and mobile application in new medical therapies and diagnostics.

5. Harness Diverse Data through Information Sciences to Improve Health Outcomes

FDA seeks to develop agency information sciences capability. Areas of interest include:

5.1 Develop and apply simulation models for product life cycles, risk assessment, and other regulatory science uses:

- 5.1.1 Identify opportunities and develop computer simulation and modeling to streamline data analysis and model biological systems and their responses to agents of concerns, such as toxins, pathogens, electromagnetic energy, and biomaterials; and
- 5.1.2 Promote novel clinical trial design using simulation, new statistical models, and novel animal models/animal model alternatives.

5.2 Analyze large scale clinical and preclinical data sets:

- 5.2.1 Refine methods for analysis of post-market data, including data mining of spontaneous reports and analysis of electronic health records from accessible large healthcare databases.

5.3 Computer Modeling and Simulation to Assess Product Risk

- 5.3.1 Develop new approaches to assess the risk of new tobacco products that will potentially enter the market by considering how such products are likely to harm, or potentially harm the users of this product based on demographic attributes of the users and usage patterns.
- 5.3.2 Develop novel methods to model the carcinogenicity, toxicity, and contribution to adverse health conditions of each component in a tobacco product based on available data – literature, EPA, legacy nonclinical studies, or submitted studies by industry.
- 5.3.3 Develop novel methods to model the demographics of a synthetic population in terms of probability distribution curves (normal distribution) based on:
 - a. Usage of tobacco product
 - b. Race
 - c. Gender

- d. Age
- e. Body Weight
- f. Pregnancy state
- g. Family structure and position within
- h. Occupation and work premises (susceptibility to secondary ingestion)

5.3.4 Develop novel methods to display model output in both graphical and numeric formats.

5.3.5 Develop and disseminate computational models and simulations that can be used as evidence for the safety and effectiveness of medical devices; establish medical device modeling validation requirements.

5.3.6 Develop novel methods to model inputs to allow one to compare at least two products and see a change reflected on the risk summary. Changes should be able to be qualitative (e.g. moderate smoker translated into 20 cigarettes per day) or quantitative (e.g. 40 cigarettes per day).

Changeable parameters should include:

- a. Type of product (average US, brand A, and/or brand B – as well as others when present in the database)
- b. Group of chemicals (e.g. vapor phase versus particulate phase)
- c. Concentration in the smoke (mean, maximum, etc)
- d. Cigarette intake rate – cigarettes per day (i.e. 5, 10, 20, 40, etc)
- e. Exposure frequency - How frequently a user is exposed (i.e. daily, one time per week, five days per month etc)
- f. Exposure duration – How long a person smokes (in years)
- g. Body weight (i.e. Caucasian male, Asian female, etc.)
- h. Averaging time – Lifespan for a given population (differing population dynamics)

6. Implement a New Prevention-Focused Food Safety System to Protect Public Health

Food Safety Modernization Act (FSMA) mandates a new approach to FDA's current food safety system, emphasizing prevention and risk-based priority setting and resource allocation to address the challenges of the modern food safety environment. Although prevention is paramount, enhanced response and investigation efforts to foodborne outbreaks when they occur, is also critical. To effectively implement this new food safety mandate, it is imperative that FDA ensures

a strong science infrastructure that clearly identifies its research needs and collaborates with other public health and research agencies in the Federal government, state government agencies, academia, and private industry. Areas of interest include:

6.1 Establish and implement centralized planning and performance measurement processes:

6.1.1 Harmonize microbiological and chemical analytical methods development and validation across the Foods Program to enhance detection and removal of unsafe contaminants from the Nation's food and feed supply.

Note: Improved, validated rapid methods, with high levels of sensitivity and specificity, would enable FDA investigators and laboratories to quickly and accurately identify sources of contamination throughout the food supply chain, thereby protecting public and animal health. In addition, improved methods would also provide defensible data to show food products are free from microbial and chemical hazards and reduce the number of unnecessary recalls which currently result in significant repercussions for industry, consumers and FDA. Research that gives FDA validated, practical and usable regulatory tools would be of great benefit in making regulatory decisions or providing guidance to industry. By sharing and leveraging resources, FDA would like to keep pace with new food technologies, the expanding array of foods in the marketplace, and identifying emerging hazards such as new pathogens and chemical contaminants that would require strategic investments in regulatory science and review.

6.2 Maintain mission critical science capabilities:

6.2.1 Identify emerging disciplines, sciences, and technologies to mitigate future risks in food safety.

Note: The primary focus would be to advance research and development (R&D) into more rapid, sensitive and specific methods to detect, identify and quantify a variety of microbial and chemical hazards (e.g. *Listeria*, *Salmonella*, *E. coli* O157:H7, melamine, arsenic) in foods and animal feeds, as well as dietary supplements and cosmetics.

7. Facilitate Development of Medical Countermeasures (MCMs) to Protect Against Threats to U.S. and Global Health and Security

FDA seeks to facilitate development of safe and effective MCMs through both intramural research and collaboration with external partners (e.g., academia, U.S. government agencies, non- governmental organizations, and industry). FDA will conduct a review for the potential of Dual

Use as defined and in accordance with USG policy. Areas of interest include:

7.1 Develop, characterize, and qualify animal models for MCM development:

- 7.1.1 Develop and evaluate animal models for the ability to demonstrate a response to the countermeasure that will be predictive for humans, including the ability to extrapolate pharmacokinetic/pharmacodynamic (PK/PD) data and/or immune correlates of protection to determine appropriate clinical dosing ; and
- 7.1.2 Refine existing animal models for Ebola virus disease to demonstrate a response to the countermeasure that will be predictive for humans, including the ability to extrapolate pharmacokinetic/pharmacodynamic (PK/PD) data and/or immune correlates to determine appropriate clinical dosing.

7.2 Modernize tools to evaluate MCM product safety, efficacy, and quality:

- 7.2.1 Identify and evaluate methods to improve availability and reuse of personal protective equipment;
- 7.2.2 Continue to develop electronic data standards and report forms to facilitate rapid assessment of the safety and efficacy of deployed MCMs;
- 7.2.3 Develop reference materials related to relevant threat agents to facilitate development of preventive vaccines, therapeutics, and detection and diagnostic methods;
- 7.2.4 Develop and evaluate high throughput, sensitive, specific, cost-effective methods to detect threat agents, diagnose the disease or condition, and perform broad-based pathogen detection.
- 7.2.5 Refine existing technologies to improve the sensitivity, specificity, and robustness of assays used to measure Ebola medical countermeasure potency and in-process and final drug substance characteristics; and
- 7.2.6 Improve the performance and quality of existing in vitro diagnostic tests for Ebola virus disease.

7.3 Identify and qualify biomarkers of diseases or conditions:

- 7.3.1 Improve knowledge of natural history of pathophysiology of human diseases or conditions caused by Chemical, Biological, Radiological and Nuclear (CBRN) agents to identify, qualify, and evaluate biomarkers; and
- 7.3.2 Identify and qualify biomarkers that enhance the understanding of the mechanism of action of MCMs, and may provide measures of MCM product efficacy.

7.4 Enhance emergency communication:

- 7.4.1 Evaluate past risk and emergency communications to identify and improve the effectiveness of communications in a public health emergency;
- 7.4.2 Improve quality and health literacy level of FDA communication about FDA-regulated products; and
- 7.4.3 Enhance FDA's capabilities and develop new strategies to collect, monitor, and track during emergencies real time data on adverse events associated with the use of drug, biologic, and device MCMs.

8. Strengthening Social and Behavioral Science at FDA by Enhancing Audience Understanding

FDA seeks to identify and improve science-based approaches, including rapidly evolving communications technologies, to clear and effective communications on the appropriate uses

of regulated products in order to promote health and reduce harms through informed decision making by consumers and health care professionals. There are four priority areas in which FDA seeks to improve comprehension among the recipients of FDA communications. Areas of interest include:

8.1 Assessment of how communications are understood, especially among diverse audiences and populations, and methods to improve the comprehension of content, including numerical information.

8.1.1 Identify effective ways to communicate so that patients and consumers, including those with low health literacy and limited English proficiency, are informed but not alarmed, assess knowledge and understanding of risk associated with use of FDA-approved products, assess the frequency and means of changing messages in order to promote continued attention to advice that is not new but remains important, evaluate methods to identify and accommodate cultural and language differences and assess the cost of these methods to the Government, and study the impact of different formats and amounts of numerical information in FDA communications for patients, health care providers, health educators and informal caregivers.

8.2 Exploration of how FDA communications can best complement those communicated by industry to enhance audience comprehension.

8.2.1 Assess awareness of direct-to-consumer advertising among patients and consumers, including those with low literacy and limited English proficiency, develop tools for measuring the effectiveness of messages that are being communicated to the public by industry advertisements and by FDA communications.

8.3 Research to assess public understanding of the regulatory terms in use.

8.3.1 Study the impact of FDA terms on the public's ability to comprehend FDA communications, and identify explanatory strategies or alternatives. Examples of FDA terms include: "safe and effective," Over-The-Counter (OTC) monograph drugs (GRAS, GRAE, "voluntary recall," "product correction," and disclaimers like "These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease."

8.4 Evaluation of timing of release of recall or warning messages, when the messages should be changed to enhance impact, and how to communicate the end of a recall or warning.

8.4.1 Characterize how consumers, patients, and caregivers understand and use emerging information including various types of uncertainty about newly identified potential risks of products; also, evaluate the ideal frequency and means of changing messages in order to promote continued attention to advice that is not new but remains important.

8.5 Studies to increase the safety of post approval drug use

- 8.5.1 Develop innovative methods to create, facilitate and encourage research in the area of safe medication use that seeks to reduce preventable harm from drugs. Approaches could include the use of clinical studies, education, innovative messaging strategies, electronic health records, or mobile technologies.

9. Strengthening the Global Product Safety Net

Globalization has made FDA's responsibilities increasingly challenging, affecting every type of product FDA regulates. In 2002, 8 million import entry lines of FDA-regulated products arrived at our borders; in 2012, it grew to 28 million and in 2013, it's expected to be 34 million. Additionally, more and more products come from developing countries where manufacturing systems may be less sophisticated and regulatory and manufacturing oversight may be minimal. As FDA continues to transform into a public health agency fully prepared for a complex, global regulatory environment, there are 3 priority areas in which FDA seeks to improve its knowledge and capabilities to enhance its international operating model. Areas of interest include:

9.1. Advancing Global Public Health

- 9.1.1. Determine how to promote and assure implementation of the essential elements of a strong regulatory system in developing economies, including (a) determining core competencies for a regulatory workforce and components of a global regulatory workforce curriculum, (b) assessing other areas related to regulatory systems' performance including conducting, costing, and financing analyses for regulatory systems, and (c) identifying and assessing existing regulatory strengthening evaluation tools utilized by governments and international organizations.

Note: Research in this area could include advancing innovative regulatory science through the development of cutting-edge investigative, inspectional and analytical rapid-screening tools.

9.2. Leveraging and Collaborating

- 9.2.1. Determine how to best identify and leverage the efforts of public and private third parties to more effectively deploy resources against risk-based priorities. This could include researching, assessing and developing recommendations regarding the landscape of existing efforts, activities, and capabilities.
- 9.2.2. Work with other public and private stakeholders to ensure that standards are well understood and applied, foster best practices in industry, and promote innovation to drive safety and quality.

- 9.2.3. Foster global coalitions of regulators by, among other actions, developing strategic approaches to the harmonization and convergence of standards, contributing to the sharing of useful information, recognition determinations, mutual reliance, and an improved ability to make appropriate regulatory decisions in real time.

Note: Research in this area could include development and use of a tool to assess the governing authorities, regulations, and operating models of various regulatory agencies in order to inform comparability determinations; and the development and use of mechanisms to share information and best practices via existing or new electronic platforms. Research might also include an assessment of the current extent of standards implementation (intended use), gaps in implementation, and priorities for broadening and harmonizing the application of standards.

9.3. Analyzing and Utilizing Global Data to Manage Risks

- 9.3.1. Define analytical methods and tools to foster improved utilization of risk analytics to inform strategies, priority-setting, and timely decision-making in the areas of inspections, training, regulatory cooperation and surveillance.
- 9.3.2. Develop predictive risk models that treat like risks in like ways across the supply chain regardless of the origin of the product.
- 9.3.3. Adopt new approaches to better aggregate and analyze multiple sources of information to fully identify risks and emerging trends based on comprehensive assessments of existing information platforms. The developed approach should include data mining of intelligence related sources (event reporting, testing results, alerts, customer complaints, news reports) to enable statistical analysis of correlations and threats. As an extension, integrate intelligence-based threat analysis into the risk-based allocation of inspection and testing resources.
- 9.3.4. Filter and analyze external indicators/signals/environmental vulnerabilities in the supply chain from various open-source intelligence and other sources to proactively identify the need for appropriate FDA interventions.

Note: Research in this area could include the development of informatics tools to connect multiple sources of information such as regulatory, economic, environmental, political and industrial factors to detectable risk signals and emerging risk trends. It could also include the development of data collection and analysis systems for external indicators/signals/environmental vulnerabilities in the supply chain from various sources intelligence and other media to alert FDA at early onset of the need for appropriate FDA actions or interventions.

9.4. Manage Risks Related to Intentional Disruptions to Food Supply

- 9.4.1. Conduct empirically-based, quantitative analyses to evaluate the risk of intentional disruptions to the food supply system. Scenario-based risk analysis shall include evaluation of the magnitude of specific threats to each supply chain component, identification of supply chain vulnerabilities, and determination of expected consequences for each scenario.
- 9.4.2. Utilize results of the risk assessment of intentional disruptions to food supply to conduct cost-benefit analysis of proposed prevention and/or response mechanisms. Generate return-on-investment data to support decision-making and investment options.

Part II: Reporting Requirements and Deliverables

As part of the work to be performed under this BAA, the Contractor shall prepare and deliver the following reports throughout the period of performance. For all reports the Contractor shall submit electronic copies to the Contracting and Project Officer.

Reports:

1. Monthly Technical Progress Reports

On the fifteenth (15) day of each month for the previous calendar month, the contractor shall submit to the Project Officer and the Contracting Officer a Technical Progress Report. Instructions for formulating Technical Progress Reports are detailed below. The technical Progress Reports shall include project timelines and milestones summaries of product manufacturing, testing, and clinical evaluation. A Technical Progress Report will not be required for the period in which the Final Report is due. The Contractor shall submit two copies of the Technical Progress Report electronically via e-mail to the Contracting Officer and Project Officer. Any attachments to the e-mail report shall be submitted in Microsoft Word, Microsoft Excel, and/or Adobe Acrobat PDF files. Such reports shall include the following specific information:

- a. Title page containing: Technical Progress Report, the contract number and title, the period of performance or milestone being reported, the contractor's name, address, and other contact information, the author(s), and the date of submission;
- b. Introduction/Background: An introduction covering the purpose and scope of the contract effort;
- c. Progress: The report shall detail, document and summarize the results of work performed, test results, milestones achieved during the period covered and cumulative milestones achieved. Also to be included is a summary of work planned for the next two (2) reporting periods on a rolling basis;
- d. Issues: Issues resolved, new issues and outstanding issues are enumerated with options and recommendation for resolution. An explanation of any difference between planned progress and actual progress, why the differences have occurred, and, if progress activity is delinquent, and what corrective steps are planned. Revised timelines are to be included.
- e. Invoices: Summary of any invoices submitted during the reporting period.
- f. Action Items: Summary table of activities or tasks to be accomplished by certain date and by whom.
- g. Distribution list: A list of persons receiving the Technical Report
- h. Attachments: Results on the project are provided as attachments

2. Final Report: By the expiration date of the contract, the Contractor shall submit a comprehensive Final Report that shall detail, document, and summarize the results of the entire contract work. The report shall explain comprehensively the results achieved. A draft Final Report will be submitted to the Project and Contracting Officers for review and comments, then the Final Report original, copies, and an electronic file shall be submitted to the Project and Contracting Officers for distribution to the Program office.

*Note: Some reports and other deliverables are relevant to specific activities that may or may not be performed during the contract period of performance. The Contractor, Contracting Officers Representative and Contracting Officer shall agree in the final contract negotiations on which reports and other deliverables are relevant and shall be required as deliverables as determined in the negotiated Statement of Work.

These reports are in addition to other reports and deliverables that may be required in the final negotiated SOW as referenced above.

3. Invoices: Cost and Personnel Reporting, and Variances from the Negotiated Budget:
 - i. The contractor agrees to provide a detailed breakdown on invoices of the following cost categories:
 - a. Direct Labor - List individuals by name, title/position, hourly/annual rate, level of effort, and amount claimed.
 - b. Fringe Benefits - Cite rate and amount
 - c. Overhead - Cite rate and amount
 - d. Materials & Supplies - Include detailed breakdown when total amount is over \$1,000.
 - e. Travel - Identify travelers, dates, destination, purpose of trip, and amount. Cite COA, if appropriate. List separately, domestic travel, general scientific meeting travel, and foreign travel.
 - f. Consultant Fees - Identify individuals and amounts.
 - g. Subcontracts - Attach subcontractor invoice(s).
 - h. Equipment - Cite authorization and amount.
 - i. G&A - Cite rate and amount.
 - j. Total Cost
 - k. Fixed Fee (if applicable)
 - l. Total

Monthly invoices must include the cumulative total expenses to date, adjusted (as applicable) to show any amounts suspended by the Government. The contractor shall be held accountable for being in compliance with the stipulations stated in FAR 52.232-20 Limitation of Cost. Furthermore, invoices submitted under BAA awarded contracts must comply with the requirements set forth in FAR Clauses 52.232-25 (Prompt Payment) and 52.232-33 (Payment by Electronic Funds Transfer-System for Award Management) and/or applicable Far Clauses specified in the actual contract document.

Part III: Proposal Preparation and Submission

Section 1: The Application Process

The application process is in two stages as follows:

Stage 1: Complete a cover page, Quad Chart, and White Paper in accordance with the preparation guidance below. Quad Charts and White Papers shall describe the effort in sufficient detail to allow evaluation of the concept's technical merit and its potential contribution to the FDA mission. Offeror's whose Quad Chart and White Paper receive a favorable evaluation may be invited to submit a Full Proposal. Offeror's whose Quad Chart and White Paper did not receive a favorable evaluation will be notified by email and will be informed of what technical issues the product needs for further FDA consideration.

Stage 2: Submit Full Proposals in accordance with the instructions provided in Section 5 below. Full Proposals will be evaluated against criteria as described in Part IV. Full Proposals that do not conform to the requirements outlined in the BAA or in the invitation will not be reviewed or considered for further action.

Proposal Stage	Deadline for Submission
Stage 1: Quad Chart and White Paper	Anytime during open period
Stage 2: Full Proposal	Within 30 calendar days of Invitation (unless designated otherwise by the CO)

Section 2: Stage 1 Quad Chart and White Paper

Interested Offeror's shall submit a White Paper which expands on the information provided in the Quad Chart. The initial submission is limited to a cover page, one-page Quad Chart (see attachment 3), White Paper not to exceed ten (10) pages, an addendum not to exceed two (2) pages and a Research and Development Justification not to exceed one (1) page, as discussed below. If submissions exceed these limitations, only those pages previously defined will be reviewed.

Combine all files and forms into a single searchable PDF file before submitting.

Quad Chart Format (One Page Limit): All quad charts shall include the information indicated on the sample template located in Attachment 3.

1. Heading: Title, Research Area Addressed, Offeror point of contact, Company's Name

2. Upper left: Objective, description of effort
3. Lower left: Benefits of proposed technology, challenges
4. Upper right: Picture or graphic
5. Lower Right: Milestones, cost, period of performance.

White Paper Technical Information (Ten Page Limit):

1. In general, the White Paper should provide a brief technical discussion of the Offeror's objective, approach, level of effort, and the nature and extent of the anticipated results. Specifically, the White Paper shall include, at a minimum, the following core elements:
 - a. brief discussion on how the proposed project aligns with the objectives of the FDA Advancing Regulatory Science Plan.
 - b. a high-level Gantt chart showing an overview of the proposed activities and timelines.
 - c. a brief description of the Offeror's intellectual property ownership of the proposed project.
 - d. an overview of the Offeror's capabilities and experience (past and current) as they relate to the proposed program.
2. The cost portion of the White Paper shall contain a brief cost estimate revealing the component parts of the proposal and a breakdown of the total cost per year.

Addendum (Two Page Limit):

As an addendum to the White Paper, include overviews (two pages total) of the key personnel who will perform the research, highlighting some of their qualifications and experience.

Justification for Research and Development (One Page Limit):

Offeror's shall submit, with the white paper package, a one (1) page justification describing how the Offeror's project falls under the FAR definition of Research and Development (See attachment 4 for details).

Restrictive markings on White Papers: Proposal submissions will be protected from unauthorized disclosure in accordance with FAR Subpart 15.207, applicable law and HHS regulations. Offeror's that include in their proposal, data that they do not want disclosed, shall mark their proposal in accordance with the instructions contained FAR 52.215-1(e) '*Restrictions on disclosure and use of data.*'

Mark the title page with the following legend:

This proposal includes data that shall not be disclosed outside the Government and shall not be duplicated, used, or disclosed—in whole or in part—for any purpose other than to evaluate this proposal. If, however, a contract is awarded to this offeror as a result of—or in connection with—the submission of this data, the Government shall have the right to duplicate, use, or disclose the data to the extent provided in the resulting contract. This restriction does not limit the Government's right to use information contained in this data if it is obtained from another source without restriction. The data subject to this restriction are contained in sheets [insert numbers or other identification of sheets]; and

Section 3: Quad Chart and White Paper Submission

White Papers shall be emailed directly to the following email address:
FDABAA@fda.hhs.gov.

Include “Research Area #_ FDABAA-15-00121 WHITE PAPER” in the email subject line. Offerors must select a primary research area to submit the white paper under even if the submission qualifies for multiple research areas. White Papers must be submitted in the following format but do not require any special forms:

- Single PDF formatted file as an email attachment
- Page Size: 8 ½ x 11 inches
- Page limit: 10 pages • Margins – 1 inch
- Spacing – single
- Font – Arial, 12 point

The file shall not exceed 2 Megabytes of storage space. Movie and sound file attachments, URL Links, or other additional files, will not be accepted.

Classification: All Quad Chart and White Paper submissions must be UNCLASSIFIED.

Notification to Offeror’s: All Offeror’s will receive an email acknowledging receipt of their Quad Chart and White Paper submission. Debriefings for Quad Chart and White Paper will not be provided, however, feedback may be provided in the response letter from FDA.

IMPORTANT NOTE: Titles given to the White Papers and Full Proposals should be descriptive of the work proposed and not be merely a copy of the title of this solicitation.

Section 4: Stage 2 Full Proposal Preparation

With a successful review of the Offeror’s White Paper, the Offeror may be invited to submit a full proposal. The Full Proposal must be prepared as two separate volumes as follows: Volume I Technical Proposal and Technical Proposal Appendices; Volume II Cost Proposal and Cost Proposal Appendices.

A. Volume I - Technical Proposal

The technical proposal page limit is 50 pages (page limitation for items 4 thru 8) of technical volume, including figures, tables and graphs unless otherwise specified by the Contracting Officer. If the proposal exceeds the number of pages specified, only the pages up to the limit will be reviewed. A page is defined as 8.5 X 11 inches, single-spaced, with one-inch margins in type no smaller than 12 point font.

1. Cover Page: This should include the words "Full Technical Proposal" and the following:
 - BAA number
 - Title of proposal
 - Identity of prime Offeror and complete list of subcontractors, if applicable
 - Technical contact (name, address, phone/fax, electronic mail address)
 - Administrative/business contact (name, address, phone/fax, electronic mail address)
 - Duration of effort
2. Official Transmittal Letter. This is an official transmittal letter with authorizing official signature.
3. Table of contents: an alphabetical/numerical listing of the sections within the proposal, including corresponding page numbers.
4. Executive Summary
5. Introduction – Overview of the project.
6. Statement of Work: The SOW should clearly detail the scope and objectives of the effort and the technical approach. It is anticipated that the proposed SOW will be incorporated as an attachment to the resultant award instrument. To that end, the proposal must include a severable, self-standing SOW, without any proprietary restrictions which can be attached to the contract or agreement award. Include a detailed listing of the technical tasks/subtasks/milestones organized by year.
7. Gantt Chart, Work Breakdown Structure and Milestones: A detailed Gantt Chart with associated Work Breakdown Structure (WBS) (Level 3) and program Milestones must be provided as part of the technical submission.
8. Deliverables: A detailed description of the results and products to be delivered inclusive of the timeframe in which they will be delivered.
9. Security Planning: The work to be performed under this contract may involve access to sensitive program information. Therefore, the Offeror(s) shall develop and submit a written Draft Security Plan that describes their procedures and policies to defend against theft, tampering, or destruction of product-related material, equipment, documents, information, and data. The Offeror is invited to submit a request for waiver if he or she believes the proposed work is exempt from some or all of the security requirements or if the Offeror can demonstrate that commensurate protective measures have been applied that afford an equal level of protection. Requests for waivers should be submitted to the Contracting Officer.
10. Intellectual Property: For issued patents or published patent applications that will be used in the performance of the contract, provide the patent number or patent application publication number, a summary of the patent or invention title, and indicate whether the Offeror is the patent or invention owner.
11. Biographical Sketches: This Section shall contain the biographical sketches for only the key personnel from both the contractor and subcontractor(s): The Full Proposal must list the names and proposed duties of the professional personnel, consultants,

and key subcontractor employees assigned to the project. Resumes shall be included in the appendices in Volume I of the Full Proposal. The resumes should contain information on education, background, recent experience, and specific or technical accomplishments as they pertain to their ability to support the objectives of this project.

12. The Offeror shall provide a list of the last three (3) government related contracts during the past three (3) years and all contracts currently being performed that are similar in nature to the BAA scope. Contracts listed may include those entered into by the Federal Government, agencies of state and local governments and commercial concerns. Offeror's may also submit past performance information regarding predecessor companies, key personnel who have relevant experience or subcontractors that will perform major or critical aspects of the requirement when such information is relevant to the proposed project. For the purposes of this BAA, a "major subcontract" is defined as a subcontract that exceeds \$25,000.

Include the following information for each contract or subcontract listed:

1. Name of Contracting Organization
2. Contract Number (for subcontracts, provide the prime contract number and the subcontract number)
3. Contract Type
4. Total Contract Value
5. Description of Requirement
6. Contracting Officer's Name and Telephone Number
7. Program Manager's Name and Telephone Number
8. North American Industry Classification System (NAICS) Code

The Offeror may provide information on problems encountered on the identified contracts and the Offeror's corrective actions.

B. Volume I – Appendices

Appendices to Volume I shall contain supplemental data that shall accompany the technical proposal. The combined page total of Appendices in Volume I is 20 pages unless specified otherwise in the full proposal invitation letter. Additional specific information to be included is referenced below. If a particular item is not relevant to the proposed effort, state that it is not applicable along with any supporting justification.

	Item	Required	Reference
1	Updated Quad Chart	Yes	Attachment 3
2	Protection of Human Subjects	If Applicable	http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html
3	Animal Use	If	See Section G below.

		Applicable	
4	Intellectual Property	Yes	
5	Biographical Sketches	Yes	
6	Use of Select Agents	If Applicable	http://www.cdc.gov/od/sap http://www.aphis.usda.gov/programs/ag_selectagent
7	Laboratory License Requirements	If Applicable	

C. Volume II – Cost Proposal

The cost proposal shall contain sufficient information for meaningful cost evaluation, and should not exceed 20 pages not including subcontractor proposals unless specified otherwise in the full proposal invitation letter. Additionally, a cost summary (not to exceed 2 pages) shall be prepared and submitted in conjunction with the detailed cost proposal. The detailed costs must readily track back to the cost presented in the summary and the WBS in the associated Project Gantt Chart. The Offeror must also provide a narrative to support the requirements in each cost element. The cost breakdown by tasks should use the same task numbering as the WBS in the Technical Proposal SOW. Options should be priced separately.

- Proposal Cover Sheet: The following information shall be provided on the first page of your pricing proposal:
 1. BAA Number;
 2. Title of proposal;
 3. Topical Area;
 4. Name and address of Offeror;
 5. Name and telephone number of the primary point of contact;
 6. Name, address, and telephone number of Contract Administration Office, (if available);
 7. Name, address, and telephone number of Audit Office (if available);
 8. Proposed cost and/or price, profit or fee (as applicable) and total cost;
 9. The following statement: By submitting this proposal, the Offeror, if selected for discussions, grants the Contracting Officer or an authorized representative the right to request and examine, at any time before award, any of those books, records, documents and/or other records directly pertinent to the information requested or submitted.
 10. Date of submission;
 11. Name, title and signature of authorized representative; and

12. DUNS number.

- **Basic Cost/Price Information:** The cost proposal shall contain sufficient information to allow the Government to perform a basic analysis of the proposed cost or price of the work. This information shall include the amounts of the line items of the proposed cost or price. The following cost elements shall be included by milestone, event or calendar year as applicable:
 - i. Direct Labor- Individual labor category or person, with associated labor hours and unburdened direct labor rates;
 - ii. Indirect Costs – Fringe Benefits, Overhead, G&A, etc. (Must show base amount and rate);
 - iii. Travel – Separated by destinations and include number of trips, durations-number of days, number of travelers, per diem (hotel and meals in accordance with the Federal Travel Regulations,), airfare, car rental, if additional miscellaneous expense is included, list description and estimated amount, etc;
 - iv. Subcontract – A cost proposal shall be submitted by the subcontractor. The subcontractor’s cost proposal shall include, on company letterhead, the complete company name and mailing address, technical and administrative/business points of contact, email address, and telephone number. Include the DUNS number. If the subcontractor’s work entails any unpredictable aspects (e.g. includes experimentation, process development, etc.) a cost proposal conforming to all requirements of this section (4.C.) shall be provided, and shall reference the WBS of the prime contractor’s proposal. If the subcontractor/vendor is providing commercially available, routine services/products (e.g. facilities audits; manufacturing from a defined protocol; off-the-shelf reagents, hardware, or software; etc.) then a less detailed price quote is allowable. In each case where the latter level of detail is provided, the Offeror shall assign subcontractor/vendor costs to the WBS, and shall be prepared to document multiple competitive quotes for the service/product.
 - v. Consultant – Provide consultant agreement or other document which verifies the proposed loaded hourly rate and labor category;
 - vi. Materials shall be specifically itemized with costs or estimated costs. Where possible, indicate pricing method (e.g., competition, historical costs, market survey, etc.). Include supporting documentation, i.e. vendor quotes, catalog price lists and past invoices of similar purchases,
 - vii. Other Direct Costs, especially any proposed items of equipment. Equipment generally must be furnished by the Offeror. Justifications must be provided when Government funding for such items is sought.
 - viii. Fee/profit including percentages.

D Volume II – Cost Proposal Appendices

Appendices to Volume II contain supplemental data of a cost and non-cost nature that should accompany the cost proposal. The combined total of Volume II appendices should not exceed 20 pages unless specified otherwise in the full proposal invitation letter. Additional specific information to be included is referenced below. If a particular item is not relevant to the proposed effort, state that it is not applicable along with any

supporting justification.

	Item	Required	Reference
1	DUNS, TIN and NAICS	Yes	
2	Representation and Certifications	Yes	FAR 4.1201
3	Security	If Applicable	
4	HHS Small Business Subcontracting Plan	If Applicable	http://www.hhs.gov/about/smallbusiness/subcontractplan.html
5	Summary of Related Activities	Yes	Attachement 1
6	Disclosure of Lobbying Activities	If Applicable	FAR 52.203-11
7	Report of Government Owned, Contractor Held Property	If Applicable	http://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/Govt-Owned-Prop.pdf

E. Representation and Certifications:

Prospective contractors shall complete electronic annual representations and certifications at SAM accessed via <https://www.sam.gov/portal/SAM/#1> as a part of required registration (see FAR 4.1102). Prospective contractors shall update the representations and certifications submitted to SAM as necessary, but at least annually, to ensure they are kept current, accurate, and complete. The representations and certifications are effective until one year from date of submission or update to SAM.

F. Studies That Involve Human Subjects

All research under this BAA must address the involvement of human subjects and protections from research risk related to their participation in the proposed research plan and comply with 32 CFR 219, 10 U.S.C. 980, and, as applicable, 21 CFR Parts 11, 50, 54, 56, 312) (45 CFR Part 46) and the ICH as well as other applicable federal and state regulations. HHS Policy also requires that women and members of minority groups and their subpopulations: children and the elderly (pediatric and geriatric) must be included in the study population of research involving human subjects, unless a clear and compelling rationale and justification is provided with

respect to the health of the subjects or the purpose of the research. The HHS policy on studies that involved human subjects can be accessible through the HHS website:

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>.

Research Projects involving humans and/or human specimens can only be initiated with written approval by the FDA Contracting Officer.

G. Animal Welfare

If the Offeror proposes to use contract funds to conduct animal studies, the Offeror must demonstrate its understanding and ability to comply with the Public Health Services (PHS) Policy on Humane Care and Use of Laboratory Animals (<http://grants.nih.gov/grants/olaw/olaw.htm>). If the Offeror has an Animal Welfare Assurance on file with the Office of Extramural Research (OER), Office of Laboratory Animal Welfare (OLAW), provide the Assurance number with the proposal. If the Offeror proposes animal studies, the Offeror must submit a plan that describes how the Offeror will comply with the PHS Policy and addresses the five points listed below:

- a. Provide a detailed description of the proposed use of the animals in the work outlined in the experimental design and methods section. Identify the species, strains, ages, sex, and numbers of animals to be used in the proposed work.
- b. Justification of the use of animals, the choice of species, and the numbers used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and their numbers.
- c. Provide information on the veterinary care of the animals involved.
- d. Describe the procedures for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. Describe the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices where appropriate to minimize comfort, distress, pain, and injury.
- e. Describe any euthanasia method to be used and the reasons for its selection. State whether this method is consistent with the recommendations of the Panel on Euthanasia of the American Veterinary Medical Association (<http://www.avma.org/resources/euthanasia.pdf>). If not, present a justification for not following the recommendations.

H. Prohibition on the Use of Appropriated Funds for Lobbying Activities HHSAR 352.270-10 Anti-Lobbying (Jan 2006):

The contractor is hereby notified of the restrictions on the use of Department of Health and Human Service's funding for lobbying of Federal, State and Local legislative bodies. Section 1352 of Title 31, United States Code (Public Law 101-121, effective 12/23/89), among other things, prohibits a recipient (and their subcontractors) of a Federal contract, grant, loan, or cooperative agreement from using appropriated funds (other than profits from a federal contract) to pay any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with any of the following covered Federal actions; the awarding of any Federal contract; the making of any Federal grant; the making of any Federal loan; the entering into of any cooperative agreement; or the modification of any Federal contract, grant, loan, or cooperative agreement. For additional information of prohibitions against lobbying activities, see FAR Subpart 3.8 and FAR Clause 52.203-12.

In addition, the current Department of Health and Human Services Appropriations Act provides that no part of any appropriation contained in this Act shall be used, other than for normal and recognized executive-legislative relationships, for publicity or propaganda purposes, for the preparation, distribution, or use of any kit, pamphlet, booklet, publication, radio, television, or video presentation designed to support, or defeat legislation pending before the Congress, or any State or Local legislature except in presentation to the Congress, or any State or Local legislative body itself as stated in P.L. 109-149, Title V, section 503(a), as directed by P.L. 110-5, Div. B, Title I, section 104.

The current Department of Health and Human Services Appropriations Act also provides that no part of any appropriation contained in this Act shall be used to pay the salary or expenses of any contract or grant recipient, or agent acting for such recipient, related to any activity designed to influence legislation or appropriations pending before the Congress, or any State or Local legislature as stated in P.L. 109-149, Title V, section 503(b), as directed by P.L. 110-5, Div. B, Title I, section 104.

I. Use of Select Agent

An HHS chaired committee of contracting, security, safety and scientific program management will assess the applicability of the facilities, regulations, policies, and procedures for meeting the U.S. requirements described in 42 CFR part 73, 7 CFR part 331, and/or 9 CFR part 121.

J. Laboratory License Requirements

The Contractor shall comply with all applicable requirements of Section 353 of the Public Health Service Act (Clinical Laboratory Improvement Act as amended). This requirement shall also be included in any subcontract for services under the contract.

K. Data Rights Clause

All contracts awarded as a result of this BAA shall be subject to FAR 52.227-14 Rights in Data – General and any other data rights clause that the FDA deems necessary for the work being conducted.

L. Advanced Understandings

1. Publications: Any manuscript or scientific meeting abstract containing data generated under this contract must be submitted for FDA Project Officer review no less than thirty (30) calendar days for manuscripts and fifteen (15) calendar days for abstracts before submission for public presentation or publication. Contract support shall be acknowledged in all such publications. A "publication" is defined as an issue of printed material offered for distribution or any communication or oral presentation of information.

2. Press Releases: The Contractor agrees to accurately and factually represent the work conducted under this contract in all press releases. Misrepresenting contract results or releasing information that is injurious to the integrity of FDA may be construed as improper conduct. Press releases shall be considered to include the public release of information to any medium, excluding peer-reviewed scientific publications. The contractor shall ensure that the Project Officer has received an advance copy of any press release related to this contract not less than

four (4) working days prior to the issuance of the press release.

3. Export control notification: Offeror's are responsible for ensuring compliance with all export control laws and regulations that maybe applicable to the export of and foreign access to their proposed technologies. Offeror's may consult with the Department of State with any questions regarding the International Traffic in Arms Regulation (ITAR) (22 CFR Parts 120-130) and /or the Department of Commerce regarding the Export Administration Regulations (15 CFR Parts 730-774).

4. Manufacturing Standards: The Good Manufacturing Practice Regulations (GMP)(21 CFR Parts 210-211) and regulations pertaining to biological products (21 CFR Part 600) and regulations pertaining to diagnostic products (21 CFR Part 860) will be the standard to be applied for manufacturing, processing, packaging, storage and delivery of this product.

*Note: If at any time during the life of the contract, the Contractor fails to comply with GMP in the manufacturing, processing, packaging, storage, stability and other testing of the manufactured drug substance or product and delivery of this product and such failure results in a material adverse effect on the safety, purity or potency of the product (a material failure) as identified by the FDA, the Offeror shall have thirty (30) calendar days from the time such material failure is identified to cure such material failure. If the Offeror fails to take such an action to the satisfaction of FDA Project Officer within the thirty (30) calendar day period, then the contract may be terminated.

5. Prohibition on contractor Involvement with Terrorist Activities: The Contractor acknowledges that U.S. Executive Orders and Laws, including but not limited to Executive Order 13224 and Public Law 107-56, prohibit transactions with, and the provision of resources and support to, individuals and organizations associated with terrorism. It is the legal responsibility of the contractor to ensure compliance with these Executive Orders and Laws. This clause must be included in all subcontracts issued under this contract.

6. Subcontracting Plans: Successful contract proposals that exceed \$650,000, submitted by all but small business concerns, will be required to submit a Small Business Subcontracting Plan in accordance with FAR 52.219-9.

7. Identification and Disposition of Data: the Contractor shall be required to provide certain data generated under this contract to the FDA. FDA reserves the right to review any other data determined by FDA to be relevant to this contract. The contractor shall keep copies of all data required by the FDA relevant to this contract for the time specified by the FDA.

8. Confidentiality of Information: The following information is covered by HHSAR Clause 352.224-70, confidentiality of Information (January 2006): Data obtained from human subjects.

Section 5: Full Proposal Submission

Full proposals must be emailed to FDABAA@FDA.HHS.GOV by the date specified in the invitation letter. If the full proposal attachments exceed the size limitation for email the offeror shall contact the contracting officer to arrange for other delivery methods.

Offeror's shall include in the Full Proposal Cover Sheet:

- The name, title, mailing address, telephone number, and fax number of the company or organization;
- The name, title, mailing address, telephone number, fax number, and e-mail address of the division point of contact regarding decisions made with respect to the Offeror and who can obligate the proposal contractually;
- The name, title, mailing address, telephone number, fax number, and e-mail address and those individual(s) authorized to negotiate with the USG; and
- A statement indicating you are submitting a Full Proposal for consideration.

*Note: Each volume of the proposal must be submitted as a separate and searchable Portable Document File (PDF) compatible with Adobe Acrobat version 7.0 or earlier.

Withdrawal of Proposals:

1. A proposal may be withdrawn by written notice received at any time prior to contract award. Withdrawals are effective upon receipt of notice by the Contracting Officer via email.
2. The government may reject Full Proposal submissions that are deemed non-compliant, i.e., that significantly deviate from the instructions in the Broad Agency Announcement or invitation to submit a full proposal.

Information to be requested from Successful Offerors: Offerors whose proposals are selected for potential award will be contacted to provide additional administrative information if required for award. Such information may include explanations and other information applicable to the proposed award.

Offeror's that are not responsive in a timely manner to Government requests for information (defined as meeting Government deadlines established and communicated with the request) may be removed from award consideration. Offeror's that request significant revisions to their proposal subsequent to their selection for potential award may be removed from award consideration. Offeror's may also be removed from award consideration if the Offeror and the Government fail to negotiate mutually agreeable terms within a reasonable period of time.

All proposals are treated as privileged information prior to award and the contents are disclosed only for the purpose of evaluation. The Offeror must indicate any limitation to be placed on disclosure of information contained in the proposal.

Section 6: General Information

PRELIMINARY INQUIRIES: FDA realizes that the preparation of a research proposal often represents a substantial investment of time and effort by the Offeror. Therefore, in an attempt to minimize this burden, FDA encourages organizations and individuals interested in submitting research proposals to make preliminary inquiries as to the general need for the type of research

effort contemplated before expending extensive effort in preparing a detailed research proposal or submitting proprietary information. The email inquiries should specify one of the subtopics from the "Research Areas of Interest" section in the subject line and shall contain one or two paragraphs on the Offeror's approach, the project goals and the approximate amount of funding needed for the project. All inquiries shall be sent in writing to FDABAA@fda.hhs.gov and will be forwarded to the appropriate technical contact.

CLASSIFIED SUBMISSIONS: Classified proposals will not be accepted.

USE OF COLOR IN PROPOSALS: All proposals received shall be stored as electronic images. Electronic color images require a significantly larger amount of storage space than black-and-white images. As a result, Offerors' use of color in proposals should be minimal and used only when absolutely necessary for details. Do not use color if it is not necessary.

POST EMPLOYMENT CONFLICT OF INTEREST: There are certain post-employment restrictions on former federal officers and employees, including special government employees (Section 207 of Title 18, U.S.C.). If a prospective Offeror believes a conflict of interest may exist, the situation should be emailed to the Contracting Officer, prior to expending time and effort in preparing a proposal. The appropriate FDA personnel will discuss any conflict of interest with prospective Offeror's.

UNSUCCESSFUL PROPOSAL DISPOSITION: Unless noted in an Offeror's proposal to the contrary, unsuccessful full proposals will be disposed of in accordance with FDA regulations.

Part IV: Proposal Evaluation

A. Evaluation Criteria:

The selection of one or more sources for award will be based on an evaluation of each Offeror's Quad Chart and White Paper and Full Proposal. The Quad Chart and White Paper and Full Proposal will be evaluated by a peer or scientific review process and will be evaluated based on the following criteria. Sub-criteria listed under a particular criterion are of equal importance. The following criteria are in descending order of importance:

1. Scientific and Technical Merit:

- Overall scientific and technical merit of the proposal
- The degree of innovation and potential to offer a revolutionary increase in capability or a significant reduction in cost commensurate with the potential risks of the innovative approach.
- The soundness, feasibility, and validity of the proposed plans, methods, techniques, and procedures of the technical proposal.
- The Offeror's understanding of the scope and the technical effort needed to address it.
- The reasonableness of the proposed schedule.

2. Importance to Agency Programs in providing foundational research that would promote research investment in applying technology, process improvements or policy solutions that could lead to significant innovations and align with FDA Regulatory Science Plan (<http://www.fda.gov/ScienceResearch/SpecialTopics/RegulatoryScience/ucm267719.htm>).

3. Capabilities and Experience:

- Overall capabilities, including the qualifications, capabilities, and experience of the proposed principal investigator, team leader, and key personnel who are critical in achieving the proposal objective; the Offeror's qualifications, capabilities, and experience in related technical areas; and the Offeror's facilities and demonstrated ability for achieving the proposal objectives. For proposals involving prototype development this will include availability (either in-house, through subcontract, or through industrial affiliates) of design and development tools/capabilities appropriate to the proposed prototype.
- Research Management: Overall capability to manage the effort, including plans to objectively measure the value and impact of the research and ensure value whether the inquiry leads or does not lead to anticipated results.
- Partnership: Degree to which the proposal develops partnerships with public and private sector entities. Significant partnering is an essential aspect of this program. Successful research teams often include entities or researchers who traditionally have not been involved in partnering with entities or researchers who have. For contract awards to be made to large businesses, the socio-economic merits of each proposal will be evaluated, but not scored, based on the extent of the Offeror's commitment in providing meaningful subcontracting opportunities for small businesses, small disadvantaged businesses, woman-owned businesses, service

disabled veteran- owned small businesses, Hub-zone small business concerns, historically black colleges and universities, and minority institutions.

B. Past Performance Information

Past performance information will be evaluated to the extent of determining the Offeror's risk of successful contract performance.

The Government is not required to contact all references provided by the Offeror. Also, references other than those identified by the Offeror may be contacted by the Government to obtain additional information that will be used in the evaluation of the Offeror's past performance.

C. Cost Evaluation

Total Cost and Cost Realism

Each price / cost response will be reviewed for price / cost realism, reasonableness, and overall best value to the Government. Members of the review team may presume that the technical approach provided by the Offeror serves as a rationale for the labor mix and labor hours used.

Applicants must adequately address the following requirements:

- a. Research involving Human Subjects/Anatomical Substances (if proposed).
- b. Research involving Animals (if proposed).
- c. Evidence of GLP Compliance (if appropriate).
- d. Evidence of GMP Compliance (if appropriate).
- e. Evidence of GCP Compliance (if appropriate).
- f. Evidence of Laboratory Licensure Requirements (if appropriate)
- g. Use of Select Agents (if appropriate)
- h. All required Representations and Certifications are completed and on file.

Throughout the evaluation of full proposals Offeror's may be asked to submit, to the Contracting Officer or Specialist, additional information and/or supporting documentation on the breakdown of costs in a full proposal. This information will be used to conduct a cost or price analysis necessary to justify that all costs in a proposal are fair and reasonable. Offeror's must comply with requests for cost and pricing information to be considered for award.

Award Decision

The final evaluation will be based on an assessment of the overall best value to the government as it relates to the criteria above. Awards, if any, will be made considering the proposal evaluation, funds availability, and other programmatic considerations.

Part V: Attachments

Attachment 1: Summary of Related Activities

The following specific information must be provided by the Offeror pertaining to the Project Director, Principal Investigator, and each of any other proposed key professional individuals designated for performance under any resulting contract.

- a. Identify the total amount of all presently active federal contracts/cooperative agreements/grants and commercial agreements citing the committed levels of effort for those projects for each of the key individuals* in this proposal.

Professional's Name and Title/Position:

<u>Identifying Number</u>	<u>Agency</u>	<u>Total Effort Committed</u>
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- 1.
- 2.
- 3.
- 4.

*If an individual has no obligation(s), so state.

- b. Provide the total number of outstanding proposals, exclusive of the instant proposal, having been submitted by your organization, not presently accepted but in an anticipatory stage, which will commit levels of effort by the proposed professional individuals*.

Professional's Name and Title/Position:

<u>Identifying Number</u>	<u>Agency</u>	<u>Total Effort Committed</u>
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- 1.
- 2.
- 3.
- 4.

*If no commitment of effort is intended, so state.

- c. Provide a statement of the level of effort to be dedicated to any resultant contract awarded to your organization for those individuals designated and cited in this proposal.

<u>Name</u>	<u>Title/Position</u>	<u>Total Proposed Effort</u>
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- 1.
- 2.

Attachment 2: Government Notice for Handling Proposals

NOTE: This Notice is for the Technical Evaluation Review Panel who will be reviewing the proposals submitted in response to this BAA. THE OFFEROR SHALL PLACE A COPY OF THIS NOTICE BEHIND THE TITLE PAGE OF THE TECHNICAL PROPOSAL.

This proposal shall be used and disclosed for evaluation purposes only, and a copy of this Government notice shall be applied to any reproduction or abstract thereof. Any authorized restrictive notices which the submitter places on this proposal shall be strictly complied with. Disclosure of this proposal outside the Government for evaluation purposes shall be made only to the extent authorized by, and in accordance with, the procedures in HHSAR 352.215-1.

- (f) If authorized in agency implementing regulations, agencies may release proposals outside the Government for evaluation, consistent with the following:
 - (1) Decisions to release proposals outside the Government for evaluation purposes shall be made by the agency head or designee;
 - (2) Written agreement must be obtained from the evaluator that the information (data) contained in the proposal will be used only for evaluation purposes and will not be further disclosed;
 - (3) Any authorized restrictive legends placed on the proposal by the prospective Contractor or subcontractor or by the Government shall be applied to any reproduction or abstracted information made by the evaluator;
 - (4) Upon completing the evaluation, all copies of the proposal, as well as any abstracts thereof, shall be returned to the Government office which initially furnished them for evaluation; and
 - (5) All determinations to release the proposal outside the Government take into consideration requirements for avoiding organizational conflicts of interest and the competitive relationship, if any, between the prospective Contractor or subcontractor and the prospective outside evaluator.
- (g) The submitter of any proposal shall be provided notice adequate to afford an opportunity to take appropriate action before release of any information (data) contained therein pursuant to a request under the Freedom of Information Act (5 U.S.C. 552); and, time permitting, the submitter should be consulted to obtain assistance in determining the eligibility of the information (data) in question as an exemption under the Act. (See also Subpart 24.2, Freedom of Information Act.)

Attachment 3: Quad Chart and White Paper Format Template

I. Quad Chart Template

Any quad chart submitted that exceeds the one-page limit will not be evaluated. Please note that the Title of the Project should be different than that of the Topic.

TITLE OF PROJECT, RESEARCH AREA ADDRESSED, PROGRAM DIRECTOR/MANAGER,
COMPANY NAME

<p><u>Objective:</u> Clear, concise (2-3 sentences) description of the objectives and methodologies of the effort.</p> <p><u>Description of effort:</u> A bullet list (2-3) of the primary scientific challenges being addressed</p>	<p>Picture or Graphic that Illustrates the research or concept (e.g. data figures, molecule illustrations or processes)</p>
<p><u>Benefits of Proposed Technology:</u></p> <p><u>Challenges:</u></p> <p><u>Research and Development Justification:</u></p>	<p><u>Bullet list of the major goals/milestones by Project Year</u></p> <p><u>Proposed Funding</u> Base period cost plus each option period (no more than 5 years total)</p> <p>Contact Information (name, email, phone)</p>

White Paper Technical Information:

1. In general, the white paper should provide a brief technical discussion of the Offeror's objective, approach, level of effort, and the nature and extent of the anticipated results. Specifically, the white paper should include, at a minimum, the following core elements:
 - a. brief discussion on how the proposed project aligns with the objectives of FDA Regulatory Science
 - b. a clear, concise development plan for licensure that includes all non-clinical, clinical, manufacturing, and regulatory activities (i.e. as applied to the FDA's animal rule) required for the proposed countermeasure.
 - c. a high-level Gantt chart showing an overview of the proposed activities and timelines.
 - d. a brief description of the Offerors intellectual property ownership of the proposed countermeasure.
 - e. overview of Offeror's capabilities and experience (past and current) as they relate to the proposed program.
2. The cost portion of the White Paper shall contain a brief cost estimate revealing all the component parts of the proposal.

3. As an addendum to the White Paper, include biographical sketches (two pages) of the key personnel who will perform the research, highlighting their qualifications and experience.
4. Offerors shall include a brief justification describing how the project falls under the FAR requirements for R&D work.

Restrictive markings on White Papers: Proposal submissions will be protected from unauthorized disclosure in accordance with FAR Subpart 15.207, applicable law and HHS regulations. Offerors that include in their proposal data that they do not want disclosed shall mark their proposal in accordance with the instructions contained FAR 52.215-1(e) *“Restrictions on disclosure and use of data”*. *Please note that any white paper submitted under this solicitation may be shared with other government agencies for non-FDA funding considerations.*

Attachment 4: Research and Development Justification

Broad Agency Announcements, as described in the Federal Acquisition Regulations (FAR), may only be issued for the procurement of Research and Development (R&D). The following are FAR definitions for Basic and Applied research and Development. All acquisitions resulting from this announcement must meet one or more of the FAR definitions below. All offerors shall write a justification describing why and how the proposal being submitted falls under one or more of the definitions for basic research, applied research and development. The justification shall be no longer than one (1) page in length, single spaced, using 12 point font.

- Basic research - Research directed toward increasing knowledge in science. The primary aim of basic research is a fuller knowledge or understanding of the subject under study, rather than any practical application of that knowledge (FAR 2.101(b)(2))
- Applied research - The effort that (a) normally follows basic research, but may not be severable from the related basic research; (b) attempts to determine and exploit the potential of scientific discoveries or improvements in technology, materials, processes, methods, devices, or techniques; and (c) attempts to advance the state of the art. When being used by contractors in cost principle applications, this term does not include efforts whose principal aim is the design, development, or testing of specific items or services to be considered for sale; these efforts are within the definition of “development,” given below (FAR 35.001).
- Development - The systematic use of scientific and technical knowledge in the design, development, testing, or evaluation of a potential new product or service (or of an improvement in an existing product or service) to meet specific performance requirements or objectives. It includes the functions of design engineering, prototyping, and engineering testing; it excludes subcontracted technical effort that is for the sole purpose of developing an additional source for an existing product and the development of a specific system or hardware procurement (See FAR 35.001).