



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-N-1269]

Collaboration in Regulatory Systems Strengthening and Standardization Activities to Increase Access to Safe and Effective Biological Products

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) announces its intention to accept and consider a single source application for award of a cooperative agreement to the World Health Organization (WHO) in support of collaboration in regulatory systems strengthening, development of norms and standards, and innovative research to advance global access to safe and effective biological products that meet international standards. The goal of FDA's Center for Biologics Evaluation and Research (FDA/CBER) is to enhance technical collaboration and cooperation between the FDA, WHO, and its member states to facilitate strengthening regulatory capacity and support product development and standardization activities to increase access to safe and effective biologics globally.

DATES: The application due date is July 5, 2016.

ADDRESSES: Submit electronic applications to <http://www.grants.gov>. For more information, see section III of the SUPPLEMENTARY INFORMATION section of this notice.

FOR FURTHER INFORMATION CONTACT: Gopa Raychaudhuri, CBER Liaison to WHO, Office of the Director, Food and Drug Administration, 10903 New Hampshire Ave., Bldg.71, rm. 7250, Silver Spring, MD 20993, 240-402-8000, gopa.raychaudhuri@fda.hhs.gov; or Leslie

Haynes, Foreign Regulatory Capacity Building Coordinator, International Affairs, Office of the Director, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 7222, Silver Spring, MD 20993, 240-402-8074, leslie.haynes@fda.hhs.gov; or Bryce Jones, Grants Management Specialist, Division of Acquisition and Grants, Office of Acquisitions and Grants Services, Food and Drug Administration, 5630 Fishers Lane, rm. 2026, Rockville, MD 20857, 240-402-2111, Bryce.Jones@fda.hhs.gov.

For more information on this funding opportunity announcement (FOA) and to obtain detailed requirements, please refer to the full FOA located at <http://www.grants.gov>. Search by Funding Opportunity Number: RFA-FD-16-044.

SUPPLEMENTARY INFORMATION:

I. Funding Opportunity Description

RFA-FD-16-044

93.103

A. Background

WHO is the directing and coordinating authority on international health within the United Nations' (UN) system. It is responsible for providing leadership on global health matters, shaping the health research agenda, setting norms and standards, articulating evidence-based policy options, providing technical support to countries, and monitoring and assessing health trends. WHO assists countries in building capacity to increase and sustain access to medical products to prevent, detect, and treat communicable diseases, including reducing vaccine-preventable diseases. WHO also coordinates efforts to respond to public health emergencies by monitoring the health situation, undertaking risk assessments, identifying priorities, and providing technical guidance and other forms of support to countries and regions.

Providing adequate regulatory oversight throughout the product life cycle (pre- and post-licensure) is essential for assuring the safety, purity, and potency of vaccines and other biologicals. However, this is a major challenge for many National Regulatory Authorities (NRAs) confronted by a steadily increasing number of novel products, complex quality concerns, new regulatory issues arising from rapid technical and technological advances, and emerging infectious diseases (e.g., pandemic influenza, Middle East Respiratory Syndrome, Ebola, Zika). WHO has an important role in strengthening regulatory systems and other supportive activities to increase access to high quality, safe, and effective biological products especially in low-and-middle-income countries. It is the only organization with the mandate, access to technical expertise, and broad reach to meet the research objectives.

FDA/CBER has been a leader and active participant in the global community to improve human health in the world's populations over many years. Its international engagements have been informed by the knowledge that protection of global public health against infectious disease threats translates into protection of public health in the United States. FDA, through CBER, has longstanding collaborations with WHO in the area of biologicals (vaccines, blood and blood products, relevant in vitro diagnostics, and cell and tissue therapies).

FDA/CBER has been a Pan American Health Organization/WHO Collaborating Center for Biological Standardization since 1998 with the current commitment running until 2020 and expectation of future extensions. As a WHO Collaborating Center for Biological Standardization, CBER has provided scientific and technical support to WHO for development of international standards, strengthening regulatory systems, advancing product safety and vigilance, vaccine prequalification, and research activities to advance development and improve standardization of vaccines and other biologicals. These areas of collaboration reflect

FDA/CBER's longstanding commitment to increasing global access of high quality, safe and effective biological products that meet international standards.

1. Development of Norms and Standards

WHO plays a key role in establishing the WHO International Biological Reference Preparations and in developing WHO guidelines and recommendations on the production and control of vaccines and other biological products and technologies. The WHO Expert Committee on Biological Standardization (ECBS) is commissioned by WHO to advise the Organization on international standards setting activities. These norms and standards are based on wide scientific consultation and on international consensus and are intended to ensure the consistent quality and safety of biological products and related in vitro diagnostic tests worldwide.

Blood products are inherently variable due to the nature of the source materials as well as the methods used to test them. The objective is to ensure that only blood products of acceptable quality, safety, and efficacy are used in the patient population. Similarly, ensuring the quality, safety, and effectiveness of vaccines is one of WHO's highest priorities. The WHO works in close collaboration with the international scientific and professional communities, regional and national regulatory authorities, manufacturers, and expert laboratories worldwide to ensure that global standards are developed and made readily available to assess the quality, safety, and effectiveness of biological products, and to support monitoring safety throughout the product life cycle.

2. Regulatory Systems Strengthening

NRAs play a vital role in the national health care system. Providing regulatory oversight throughout the product life cycle (pre- and post-licensure) is a major challenge for many NRAs

confronted by a steadily increasing number of novel products, complex quality concerns, new regulatory issues arising from rapid technical and technological advances, and emerging infectious diseases (e.g., pandemic influenza, MERS, Ebola, Zika). WHO has an important role in strengthening regulatory systems to increase access to high quality, safe, and effective biological products especially in low-and-middle-income countries. In this era of globalization, establishment of robust regulatory systems in other regions of the world also benefits the U.S. population as it facilitates FDA's ability to better monitor and ensure the safety of the supply chain for medical and other products entering the United States from other countries.

3. WHO Prequalification Program

The WHO prequalification program was established in response to the need to supply quality health products, including vaccines and in vitro diagnostic tests for the prevention, diagnosis, and treatment of priority diseases in low-and-middle-income countries. Through the prequalification program, WHO assures the quality, safety, and effectiveness/performance of these products, and suitability for use in the target settings.

As part of the vaccine prequalification program, WHO provides advice to the United Nations Children's Fund (UNICEF) and other UN agencies on the acceptability, in principle, of vaccines considered for purchase by such agencies for vaccination programs they administer. An important part of the vaccine prequalification program is WHO's reliance upon a stringent NRA to provide regulatory oversight of the vaccine throughout the product's life cycle. In 2009, FDA entered into a confidentiality arrangement with WHO to enable FDA/CBER to serve as a NRA of record in the vaccine prequalification program and currently serves in this capacity for nine U.S. licensed, WHO prequalified vaccines.

4. Product Safety and Vigilance

The safety of medical products depends on a variety of factors that range from good manufacturing practices to strong national systems able to monitor the products in domestic markets. However, with increasing globalization of trade, overall effective surveillance of medical products depends on international regulatory cooperation and information sharing. WHO promotes the global safety of medical products by coordinating global networks for information sharing, such as data bases and monitoring and alert systems, and by supporting countries to develop national capacities for the post-marketing surveillance of biological products.

WHO and partners have developed a strategic framework (“Global Vaccine Safety Blueprint”) to promote the establishment of effective vaccine pharmacovigilance systems globally. The Blueprint proposes a strategic plan for strengthening vaccine safety activities worldwide, focusing on building national capacity for vaccine safety in the world’s poorest countries through the coordinated efforts of major stakeholders.

WHO advisory bodies also play a significant role in reviewing and assessing product safety data and making recommendations to WHO regarding use of vaccines and other biological products. For example, the Global Advisory Committee on Vaccine Safety (GACVS) provides independent, authoritative, scientific advice to WHO on vaccine safety issues of global or regional concern, and the Blood Regulators’ Network (BRN) serves as an advisory body to WHO on matters related to safety and availability of blood and blood products.

5. Regulatory Science to Promote Development and Increased Access to Safe and Effective Biological Products

Regulatory science aims to contribute to the development of new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of regulated biological

products. Examples include tools to standardize assays used for regulatory purposes (e.g., development of correlates of immunity; correlates of safety; improved methods for product characterization; new or alternative potency assays etc.). Results generated through methods and tools developed through regulatory science efforts such as adaptive clinical trial designs, benefit/risk assessment, novel pharmacovigilance methodologies, and other tools inform regulatory decisionmaking processes. Knowledge gained through regulatory science can play a significant role in regulatory decisionmaking, policy development, and preparedness to address threats from existing or emerging infectious diseases.

FDA, with other HHS technical agencies and offices, WHO, and other regulatory counterparts, are strategizing on approaches to increase access of the global population to safe and effective biological products for the prevention, diagnosis, and treatment of priority diseases, especially for use in low-and-middle-income countries. This project represents a collaborative effort between FDA and WHO (and complements and builds upon the U.S. Government's existing commitments with WHO) to support scientific collaboration and enhance regulatory capabilities of NRAs and networks to advance global access to safe and effective vaccines and other biologicals that meet international standards. This project will further support science-based and data-driven public health strategies and approaches, and lead to improved technical cooperation between FDA, WHO, and its member states.

B. Research Objectives

The project has the following goals:

1. Contribute to the Knowledge Base of the Current State of Regulatory Oversight of Vaccines and Other Biological Products

- Support NRA assessments and analyses and synthesis of the data, and development of an institutional development plan to enhance regulatory performance in low-and-middle-income countries. Assessment of regulatory systems could include but is not limited to, analyses and synthesis of existing data from assessments of vaccine regulatory capabilities of different NRAs, and new applications of assessment frameworks to specific areas, such as pharmacovigilance (e.g., monitoring safety and effectiveness of new vaccines following introduction in a specific country or regional setting). NRA assessments also support WHO's vaccine prequalification program;
- Analysis of regulatory systems performance can include assessment of challenges, risks, and emerging trends, with the aim of further strengthening the development of data/information systems as sources of inputs for evidence-based regulatory decisions and actions; and
- Expected outputs could include analyses, reports, and data-driven strategy papers, among others.

2. Providing Technical Support to Regulatory Systems Strengthening Efforts

- Enable the strengthening of regulatory systems at the national and regional levels in such critical domains as good manufacturing, clinical, and laboratory practices; monitoring and evaluation of product quality; lot release; inspection and surveillance of products throughout the supply chain; pharmacovigilance systems building and analyses; risk assessment, analysis, and management etc.;
- Support the diffusion and application of knowledge, data, and information through active participation in regional and global committees and networks, such as the African Vaccine Regulatory Forum, ECBS, GACVS, BRN etc.; and

- Expected outputs could include analyses, reports, and data-driven strategy papers, among others.

3. Development of Global Norms and Standards

- Enable the timely and effective sharing of scientific findings and data through international collaboration to develop WHO International Biological Reference Preparations and WHO guidelines and recommendations on the production and control of vaccines and other biological products and technologies;
- Assist Member States in the implementation of internationally-recognized standards and guidelines, e.g. WHO guidelines and standards and those emerging from standards development venues such as the International Council for Harmonisation of the Technical Requirements for Pharmaceuticals for Human Use;
- Utilize WHO's convening power to engage with relevant stakeholders in support of data-driven and science-based public health strategies and approaches to enhancing global regulatory capacity and cooperation; and
- Expected outputs could include guideline documents, physical standards (e.g., reference reagents, reference panels etc.), reports, and data-driven strategy papers, among others.

4. Support Regulatory Science and Other Activities to Promote Development and increased Access to Safe and Effective Biological Products

- Enable development of new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of regulated biological products;
- Support programs, including but not limited to WHO prequalification, that increase access to safe and effective biological products; and

- Expected outputs could include analyses, reports, and data-driven strategy papers, among others.

C. Eligibility Information

The following organization is eligible to apply: WHO.

II. Award Information/Funds Available

A. Award Amount

FDA/CBER anticipates providing in FY2016 up to \$2 million (total costs including indirect costs) for one award (subject to availability of funds) in support of this project. Future year amounts will depend on annual appropriations, availability of funding, and awardee performance. CBER anticipates providing four additional years of support up to the following amounts:

FY 2017: \$2 million

FY 2018: \$2 million

FY 2019: \$2 million

FY 2020: \$2 million

B. Length of Support

The support will be 1 year with the possibility of an additional 4 years of noncompetitive support. Continuation beyond the first year will be based on satisfactory performance during the preceding year, receipt of a noncompeting continuation application, and available Federal Fiscal Year appropriations.

III. Electronic Application, Registration, and Submission Information

Only electronic applications will be accepted. To submit an electronic application in response to this FOA, applicants should first review the full announcement located at

<http://www.grants.gov>. Search by Funding Opportunity Number: RFA-FD-16-044. (FDA has verified the Web site addresses throughout this document, but FDA is not responsible for any subsequent changes to the Web sites after this document publishes in the Federal Register.) For all electronically submitted applications, the following steps are required.

- Step 1: Obtain a Dun and Bradstreet (DUNS) Number
- Step 2: Register with System for Award Management (SAM)(formerly CCR)
- Step 3: Obtain Username & Password
- Step 4: Authorized Organization Representative (AOR) Authorization
- Step 5: Track AOR Status
- Step 6: Register with Electronic Research Administration (eRA) Commons

Steps 1 through 5, in detail, can be found at

<http://www.grants.gov/web/grants/applicants/organization-registration.html>. Step 6, in detail, can be found at <https://commons.era.nih.gov/commons/registration/registrationInstructions.jsp>.

After you have followed these steps, submit electronic applications to: <http://www.grants.gov>.

Dated: May 24, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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