

JOINT PROJECT MANAGER MEDICAL COUNTERMEASURE SYSTEMS



BROAD AGENCY ANNOUNCEMENT (BAA) FOR MEDICAL CHEMICAL BIOLOGICAL RADIOLOGICAL AND NUCLEAR (CBRN) COUNTERMEASURE DEVELOPMENTAL STUDIES

MCS-BAA14-01

DECEMBER 2013

I. Table of Contents

II. INTRODUCTION	4
III. ACRONYMS	6
IV. GENERAL INFORMATION	9
A. AWARDS.....	9
1. TYPE OF JPM CMS AWARDS.....	9
2. CONTRACTOR MANPOWER REPORTING	10
3. BASIC JPM-MCS AWARD PROCEDURES	11
B. CONFLICT OF INTEREST	12
C. DISCLOSURE OF INFORMATION OUTSIDE THE U.S. GOVERNMENT	12
D. U.S. GOVERNMENT OBLIGATION	12
E. INFORMATION SERVICE	12
F. PREPROPOSALS.....	12
G. FULL PROPOSALS	13
V. APPLICATION INSTRUCTIONS	14
A. GENERAL FORMATTING GUIDELINES	14
B. CONTRACTS	14
C. GRANTS.....	19
1. FULL PROPOSAL PREPARATION FOR GRANTS	20
D. REGULATIONS AND FORMS.....	21
VI. EVALUATION AND SELECTION	21
A. EVALUATION FACTORS FOR PROCUREMENT CONTRACTS AND GRANTS	21
B. SELECTION FOR PROCUREMENT CONTRACTS AND GRANTS	23
VII. AWARD ADMINISTRATION.....	23
A. PAYMENT.....	23
1. CONTRACTS	23
2. GRANTS	24
B. INFORMATION RELEASE	24
C. FREEDOM OF INFORMATION ACT REQUESTS	25
D. SITE VISITS	25
E. REPORTS/MEETINGS/KNOWLEDGE DISEMINATION	25

F.	AUDITS AND COST PRINCIPLES	26
VIII.	JPM MCS MISSION STATEMENTS AND AREAS OF INTEREST	26
A.	SCOPE OF PROPOSALS SOUGHT	26
B.	DEFINITIONS	27
C.	MEDICAL COUNTERMEASURES SYSTEM JOINT DEPUTY PRODUCT MANAGERS, ORGANIZATIONAL MISSION STATEMENTS AND BAA TECHNICAL POINTS OF CONTACT.....	28
D.	MISSION AREAS	29
1.	MEDICAL BIOLOGICAL PROPHYLAXIS	29
2.	MEDICAL CHEMICAL AND BIOLOGICAL COUNTERMEASURES	31
3.	MEDICAL RADIOLOGICAL COUNTERMEASURES.....	32
4.	MEDICAL DIAGNOSTIC AND SURVEILLANCE SYSTEMS.....	33
5.	CRITICAL REAGENTS PROGRAM (CRP).....	33
IX.	ATTACHMENTS AND APPENDICES	35

II. INTRODUCTION

The Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD) is organized into five Joint Project Management Offices (JPMO), each responsible for specific commodity areas. General information on the JPEO-CBD and subordinate JPMOs can be obtained from the JPEO-CBD website at <http://www.jpeocbd.osd.mil/>.

The medical CBRN countermeasures developed by the Joint Project Manager Medical Countermeasure Systems (JPM MCS) office, the subject of this BAA directly support the current, near-term, and far-term challenges by providing the capability to prevent, diagnose and treat the effects of chemical, radiological and biological warfare agents. Mission areas and technical points of contact for the product management offices within the JPM MCS are shown in Section VIII of this BAA. This Broad Agency Announcement (BAA) is intended to solicit pre-proposals for JPM MCS for: 1) those parts of development not related to the development of a specific system or hardware procurement in accordance with (i) the Federal Acquisition Regulation (FAR) 35.016(a) and (ii) DoD Grant Regulations (DoDGARs) subject to section 2374 of Title 10 United State Code and 2) the development of prototypes in accordance with Section 845 of Public Law (P.L.) 103-160. The purpose of this BAA is to identify the best available science, and as such, there are no set-asides associated with any awards resulting from this BAA. Specific areas of interest are described in the "Areas of Interest" section of this BAA. As to any resultant procurement contracts, this BAA is issued under the provisions of the Competition in Contracting Act of 1984 (P.L. 98-369), as implemented in the FAR. This Announcement provides a general description of JPM MCS's project areas, including specific areas of interest, general information, evaluation and selection criteria, and proposal preparation instructions. All documentation and or Attachments that are required with the submission of a full proposal are described in the Mandatory Proposal Forms section of this announcement. Proposals are sought from all eligible sources, including educational institutions, nonprofit organizations, and private industry. Generally, this announcement is continuously open; preliminary proposals (preproposals) may be submitted and will be evaluated at any time throughout the year. The availability of funds may limit the ability of the U.S. Government to make awards in specific areas, nevertheless preproposals are sought under this BAA announcement for areas consistent with the mission areas identified in Section VIII of this announcement. JPM - MCS is interested in proposals that are based on data from experiments using specific CBRN warfare agents, not surrogates, to demonstrate safety, efficacy or mode of action. (Please note that CBRN warfare agents will not be provided by the DoD for these efforts.) We are interested in studies on new and better ways to develop medical CBRN countermeasures more rapidly and with increased efficiency through enabling technologies, life cycle bioinformatics, and improved logistics tracking. We are not interested in proof-of-concept, advanced, applied or basic research proposals. We are interested in efforts directed toward the development of enabling technologies that speed up the advanced development process leading to FDA approval. All developmental efforts nominated to be considered by this BAA should be evaluated against the Quality Technology Readiness Levels (Q-TRL) (Attachment 1). Potential

developmental efforts must be consistent with the minimum criteria at TRL level 4 for transition to advanced development. In particular, the scope of work proposed under this BAA must be limited to TRL 4 levels described at 4-M1, 4-D1 and 4-E1 for Medical Products and 4-DAM1, 4-DAS1, 4-DCS1 for Diagnostics:

MEDICAL PRODUCTS:

4-M1: Demonstrate Capability to Produce the Technology in a Lab Environment. Prepare laboratory-scale non-GLP/non-cGMP quantities of BDS to further refine manufacturing process. Formulate an experimental drug product (EDP) for preliminary animal studies. Evaluate BDS and EDP for conformance to preliminary specifications.

4-D1: Conduct non-GLP safety studies to include early toxicity in animal models consistent with product's intended use (e.g. route of administration and dose range (small animals may be used)).

4-E1: Expand on initial proof of concept studies to develop relevant animal model(s). Demonstrate relevance to threat being addressed.

DIAGNOSTICS:

4-DAM1: Support assay architecture development, providing input on manufacturability of proposed product

4-DAS1: Continued animal studies, as required, to support assay development and assay design finalization.

4-DCS1: Continued pre-clinical studies, as required, to support assay development and diagnostic targets finalization.

This announcement of the JPM MCS's current interests will be posted on the Grants.gov web portal (<http://www.grants.gov/>), the Federal Business Opportunity website (<http://www.fedbizopps.gov>), Natick Contracting Division <http://www3.natick.army.mil/ssbaa.html> and the JPEO-CBD website (<http://www.jpeocbd.osd.mil/>). From time to time, this BAA may be amended with special announcements or calls for proposals. Additionally, the application process may be amended as other electronic application processes are implemented. All amendments to this BAA will be announced on the websites shown above.

To facilitate communication on both scientific and administrative matters relating to this BAA, a single email address may be used for all communication with JPM MCS. Please send all technical and administrative questions and inquiries to usarmy.detrick.cbms.mbx.baa@mail.mil.

Potential applicants are encouraged to discuss their proposal ideas with the JPM MCS technical contacts listed in Section VIII. Missions and BAA Areas of Interest.

Administrative questions concerning the preparation of preproposals or proposals should be addressed to U.S. Army Contracting Command Natick Contracting Division/ Grants Officer. They should be emailed to usarmy.detrick.cbms.mbx.baa@mail.mil, faxed to 301-619-5069, ATTN: JPM MCS BAA 14-01, or mailed to the following address:

Joint Project Manager Medical Countermeasures

ATTN: JPM MCS-BAA 14-01/ACC-APG-NCD

1564 Freedman Dr.

Ft. Detrick, MD 21702

Issues with submitting applications through the Grants.gov web portal should be directed to the Grants.gov help desk at 1-800-518-4726 or email support@grants.gov. The Contact Center hours of operation are Monday-Friday, 7 AM to 9 PM Eastern Standard Time.

The Catalog of Federal Domestic Assistance (CFDA) can be accessed online at <https://www.cfda.gov>. The online CFDA provides access to a database of all Federal programs available to the grant community, including state, local and tribal Governments, academia and research institutions, commercial firms and not-for-profits. Included on the web site are contact information for the office that administers each program, instructions on how to apply for assistance, and several proposal writing guides. The CFDA number for this announcement is 12.360.

PLEASE NOTE THAT THIS ANNOUNCEMENT IS NOT FOR THE ACQUISITION OF TECHNICAL, ENGINEERING, CONSULTING OR OTHER TYPES OF SUPPORT SERVICES

III. ACRONYMS

ACC-APG-NCD	Army Contracting Command-Aberdeen Proving Ground-Natick Contracting Division
ACO	Administrative Contracting Officer
ACURO	Animal Care and Use Review Office
AOR	Authorized Organizational Representative
BAA	Broad Agency Announcement
BLA	Biologics License Application

BWA	Biological Warfare Agent
CBDP	Chemical Biological Defense Program
CBRN	Chemical, Biological, Radiological, and Nuclear
CDRL	Contract Data Requirements List
CFDA	Catalog of Federal Domestic Assistance
CFR	Code of Federal Regulations
CLINs	Contract Line Item Numbers
cGMP	current Good Manufacturing Processes
CWA	Chemical Warfare Agent
CWBS	Contract Work Breakdown Structure
DCAA	Defense Contract Audit Agency
DCMA	Defense Contract Management Agency
DFARS	DoD FAR Supplement
DoD	Department of Defense
DoDGARs	DoD Grant and Agreement Regulations
D-U-N-S®	Data Universal Number System
EPLS	Excluded Parties List System
EFT	Electronic Funds Transfer
FAR	Federal Acquisition Regulation
FDA	U.S. Food and Drug Administration
FCCM	Facilities Capital Cost of Money
FOIA	Freedom of Information Act
FY	U.S. Government Fiscal Year, which begins October 1
GCP	Good Clinical Practices
GLP	Good Laboratory Practices

HRPO	Human Research Protection Office
IMS	Integrated Master Schedule
IND	Investigational New Drug
IAE	Integrated Acquisition Environment
JPEO-CBD	Joint Program Executive Office for Chemical and Biological Defense
JPM-MCS	Joint Project Management-Medical Countermeasure Systems
NDA	New Drug Application
NIOSH	National Institute of Occupational Safety and Health
OMB	Office of Management and Budget
OSD	Office of the Secretary of Defense
P.L.	Public Law
POC	Point of Contact
Q-TRL	Quantitative Technological Readiness Level
RDT&E	Research, Development, Test, and Evaluation
RFFP	Request for Full Proposal
R&R	Research and Related
SAM	System
SF	Standard Form
SOW	Statement of Work
TRL	Technology Readiness Level
USC	U.S. Code
WAWF	Wide-Area Work Flow
WBS	Work Breakdown Structure

IV. GENERAL INFORMATION

A. AWARDS

1. TYPE OF JPM CMS AWARDS.

The JPM CMS contemplates the award of procurement Contracts, Grants or Cooperative Agreements under this BAA in support of its mission to foster and/or conduct the advanced development of FDA-approved medical CBRN countermeasures. The purpose of this BAA is to identify the best available science, and as such, there are no set-asides associated with any awards resulting from this BAA due to the impracticality of reserving discrete or severable areas/elements of development in the cited areas of interest or to inapplicability.

Procurement contracts. Procurement contracts will be utilized to fund development activities that, while directly supporting a U.S. Government requirement, are not related to the development or procurement of a specific system. These efforts should be intended for developmental scientific study and experimentation directed toward advancing the state-of-the-art or increasing knowledge or understanding, rather than focusing on a specific system, product, or medical countermeasure. Examples of the use of a procurement contract include a Good Laboratory Practices (GLP)-compliant animal toxicology study, or a Phase 1 clinical safety study.

Grants/Cooperative Agreements. Consistent with statutory authority, funds may be awarded by CBMS JPMO to stimulate or support a public purpose consistent with the broad CBMS JPMO objectives to develop, approve, and field medical CBRN countermeasures. These efforts should be intended for scientific study and experimentation directed toward advancing the state-of-the-art or increasing knowledge or understanding, rather than focusing on a specific system, product, or medical countermeasure. These grants are typically funded with Congressional special interest funds. By submitting a proposal and accepting an award, the recipient organization is certifying that the Project Manager and other investigators' credentials have been examined and verified to ensure that the investigators are qualified to conduct the proposed study, and if applicable, to use humans or animals as research subjects in accordance with all federal and institutional guidelines and regulations. A Cooperative Agreement is used to enter into the same kind of relationship as a grant, except that substantial involvement is expected between the DoD and the recipient when carrying out the activity contemplated by the cooperative agreement. This term "Cooperative Agreement" does not include "Cooperative Research and Development Agreements" as defined in 15 USC 3710a.

No fee or profit is allowed on Grants or Cooperative Agreements awarded by the Department of Defense.

The type of instrument used to reflect the business relationship between the recipient and the U.S. Government will be determined by the Grants, Agreements, or Contracting Officer prior to award. The U.S. Army Contracting Command Aberdeen Proving Ground Natick Contracting Division, Fort Detrick (ACC-APG Natick), which provides contracting support JPM MCS, will process proposals selected for funding. Offerors may identify the type of instrument that they feel best suites the proposed effort. An Offeror's suggestion regarding suitable type of instrument does not obligate the government to employ the suggested instrument type.

The offeror shall note that, in accordance with FAR Subpart 16.301-3, in order to receive a COST type contract, their accounting system must be adequate for determining costs on a government contract. This is determined by the Defense Contract Audit Agency (DCAA) assigned to the offeror's business location and may take thirty (30) to forty (40) days for completion.

2. CONTRACTOR MANPOWER REPORTING

All contracts awarded under this BAA will include the following clause:

ACCOUNTING FOR CONTRACT SERVICES REQUIREMENT (Sep 2011)
ACC-APG 5152.237-4005

The Office of the Assistant Secretary of the Army (Manpower & Reserve Affairs) operates and maintains a secure Army data collection site where the contractor shall report ALL contractor manpower (including subcontractor manpower) required for performance of this contract. The Army's objective is to collect as much significant Contractor Man-Year Equivalents (CME) data as possible to allow accurate reporting to Congress and for effective Army planning. Detailed instructions can be found on the Contractor Manpower Reporting Application (CMRA) website in the CMRA "Contractor User Guide" or "Subcontractor User Guide". The contractor must create an account upon entering the site and is required to completely fill in the required information at the CMRA website: <https://cmra.army.mil>.

The required information includes:

- (1) Unit Identification Code (UIC) of the Army Requiring Activity that would be performing the mission if not for the contractor: _____ (*Enter the Army Requiring Activity's UIC here*).
- (2) Command of the Requiring Activity that would be performing the mission if not for the contractor: _____ [*Enter the Major Command (MACOM) of the Requiring Activity here*].
- (3) Contracting Officer (KO) and contact information: (*Enter KO's name, phone number, and email address*).
- (4) Contracting Officer's Representative (COR) and contact information: _____ (*Enter COR's name, phone number, and email address*).
- (5) Federal Service Code (FSC) reflecting services provided by contractor (and separate FSC for each subcontractor if different). If there are multiple FSCs for an Order number, enter a separate data record for each FSC.
- (6) Location where contractor and subcontractor(s) perform the service, including the city, state, zip code, and country. When service is performed at an overseas location, state only the city and country. If there are multiple Locations for an Order number, enter a separate data record for each Location. (*Note: If there are many location records that need to be entered, the Bulk Loader function is available which allows the transfer of information from a contractor's system to the secure web site. The Bulk Loader Template and Bulk Loader Instructions may be downloaded from the web site.*)
- (7) Contractor Type (prime or subcontractor).

- (8) Direct labor hours (including subcontractors) for each FSC.
- (9) Direct labor dollars paid this reporting period (including subcontractors) for each FSC.
- (10) Weapons system support indication: ____ _ (*Enter yes or no*).

If subcontractors are used in the performance of this contract, several factors must be considered. Contractor shall include, and require inclusion of, this term in all subcontracts at any tier under the contract in which services are being procured. Contractor shall also enter their data in a timely manner, as subcontractors can not input any information into the CMRA system until the Prime Contractor has entered their data. The Prime Contractor has overall responsibility for ensuring subcontractors enter their respective data. Subcontractors are only responsible for entering Location Data.

3. BASIC JPM-MCS AWARD PROCEDURES

To protect the public interest, the Federal Government ensures the integrity of Federal programs by only conducting business with responsible recipients. The ACC-APG Natick Contracting Division uses the System for Award Management (SAM) to exclude recipients ineligible to receive federal awards. Grant funds are generally awarded via cost-reimbursement or periodic scheduled payments, in accordance with the negotiated payment schedule included in the award document.

Recipient organizations should meet certain minimum standards pertaining to institutional support, financial resources, prior record of performance, integrity, organization, experience, operational controls, facilities and conformance with safety and environmental statutes and regulations in accordance with DoDGARs section 22.410 or FAR subpart 9.1.

Investigators are cautioned that awards are made to organizations, not individuals. A Project Manager must submit a proposal through, and be employed by, an organization in order to receive support. (Federally Funded Research and Development Centers are not eligible for awards in accordance with FAR 35.017-7). Should the Project Manager of a funded project leave the recipient institution, both the Project Manager and institution must contact ACC-APG Natick Contracting/Grants Officer as soon as possible to discuss options for continued support of the project. Every effort should be made to notify ACC-APG Natick prior to the Project Manager leaving the institution.

Organizations located outside of the U.S. may submit in response to the BAA, however, it is the organizations' responsibility to ensure that the project staff is able to complete the work without intercession by the DoD for a J-1 Visa Waiver on behalf of a foreign national in the United States. In addition, the U.S. Government will not provide funds to support scientists from countries which support terrorism.

Funding may be provided incrementally during the life of the award. Under cost-reimbursement type awards, payments are made in response to monthly vouchers or invoices submitted by the awardee.

As to grants and procurement contracts, the primary basis for the selection of proposals is based upon evaluation of technical merit, programmatic relevance, and the availability of funds.

Detailed information on proposal evaluation and selection is located in section III, "Evaluation and Selection."

B. CONFLICT OF INTEREST

There are certain post-employment restrictions on former Federal officers and employees as defined in 18 USC 207 and FAR 3.104-4(c). If a submitter believes a post-employment restriction or conflict of interest exists, the situation should be discussed with the JPM MCS legal staff (telephone 301-619-8444) prior to expending time and effort in preparation of a proposal.

C. DISCLOSURE OF INFORMATION OUTSIDE THE U.S. GOVERNMENT

Proposals may be disclosed outside of the U.S. Government subject matter experts for the sole purpose of technical and programmatic evaluation. The JPM MCS obtains a written agreement from the evaluators that information in the proposal will only be used for evaluation purposes and will not be further disclosed. Proposals for funded projects will be subject to public release under the Freedom of Information Act to the extent that they are incorporated into an award document; proposals that are not selected for funding will not be subject to public release.

D. U.S. GOVERNMENT OBLIGATION

Only a warranted Contracting, Grants, or Agreements Officer may obligate the U.S. Government to the expenditure of funds for awards under this BAA. The U.S. Government does not fund preparation of proposals or support work efforts or tasks that are inferred from discussions with technical project officers.

E. INFORMATION SERVICE

Submitters may use the technical reference facilities of the Defense Technical Information Center (DTIC) to acquire information of U.S. Government funded projects to avoid duplication of scientific and engineering effort. The Defense Technical Information Center (DTIC) is responsible for collecting all scientific or technological observations, findings, recommendations, and results derived from Department of Defense endeavors. Requests for eligibility and registration information should be addressed to DTIC-BC Registration, 8725 John J. Kingman Road, Ft. Belvoir, VA 22060-6218, or may be obtained at <http://www.dtic.mil>.

F. PREPROPOSALS

Organizations are strongly encouraged to explore JPM MCS interest by submitting a preliminary proposal (preproposal). Preproposals may be submitted at any time describing a specific idea or project that pertains to any of the advanced development areas of interest outlined in the BAA. Preproposals should be no longer than three pages, and include a description of the relevant technology including supporting data, the scope of the proposed effort including a high-level Work Breakdown Structure (WBS), and a description of the proposer's research, development, manufacturing, past performance, or other special qualifications. The preproposal should include

an anticipated cost for the efforts described in the preproposal. Preproposals may be submitted to the following email address: usarmy.detrick.cbms.mbx.baa@mail.mil. Brochures or other descriptions of general organizational or individual capabilities will not be accepted as a preproposal. All preproposals will be assigned an identification number and an email or postcard will acknowledge receipt of a preproposal. Usually, the Project Manager of the submitting organization should receive a decision letter or email regarding the preproposal within 60-90 days of submission.

In accordance with the United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern (DURC) released 29 March 2012, research being proposed which falls under the definition of DURC, “life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security”, must be identified in the Offeror’s preproposal. If a full proposal is then requested by the Government, risk mitigation of this concern shall be included as part of the Risk Management Plan of the Technical proposal section (see section V.B.3.e) of this document.

G. FULL PROPOSALS

If the preproposal for a procurement contract is accepted, ACC-APG Natick Contracting Division will send the a Request For Full Proposal (RFFP) and any additional requirements, including suggested Contract Line Item Numbers (CLINs), a Contract Data Requirements List (CDRL), clauses, terms, and conditions. Full proposals shall be submitted within 45 days after being requested. The U.S. Government reserves the right to reject submissions received more than 45 days after the request for a full proposal from the U.S. Government. Receipt of full proposals will be acknowledged by email or postcard. The Proposal Log Number for the full proposal will be the same number used for the preproposal (if one was submitted).

To apply for a grant, the forms identified for the JPM MCS BAA on the Grants.gov web portal must be completed and included as part of the submission for a full proposal. Full proposals may be submitted without protocols for human and animal use. However, protocols with required institutional approvals must be submitted not later than 60 days after award to demonstrate continued progress and ensure continuation of payment. The contracting office may make exceptions in situations where human and/or animal use is not expected to begin until after the first year of the award. In such cases, a time frame for submission of the appropriate protocols should be established during discussions/negotiations, prior to award.

There are no specified funding limitations identified for the proposals submitted under the JPM MCS BAA. The budget should be commensurate with the nature and complexity of the proposed effort. An award decision should be forwarded by the U.S. Government within 180

days after submission. Be advised that at the time of publication of this BAA there are no funds identified for award, and any award(s) are predicated on the availability of funds.

V. APPLICATION INSTRUCTIONS

A. GENERAL FORMATTING GUIDELINES

Applications for all types of awards under this BAA (grant, procurement contract) shall be clear and legible, and must conform to the following general formatting guidelines:

1. Elaborate proposals with high-gloss paper, vivid colors, detailed artwork, or other embellishments are unnecessary and not desired.
2. Paper: Pages shall be 8.5 x 11 inches, single sided, with each page numbered "X of Y pages."
3. Margins: Minimum of 1 inch on all sides.
4. Type Font: 12 point Times New Roman, single spaced.
5. Contract Work Breakdown Structure (CWBS) and Integrated Master Schedule (IMS)/Gantt Charts: The minimum CWBS expected is Level 4. The IMS shall document the critical path and predecessor tasks.
6. Acronyms: Spell out all acronyms the first time they are used. One page of the proposal body is allocated to spell out acronyms, abbreviations and symbols.
7. Language: English.
8. Electronic file format: PDF, compatible with Adobe Acrobat Reader v. 8.0. File size less than 20 MB.

B. CONTRACTS

If a preproposal submitted in response to this BAA is accepted by the U.S. Government, a Request for Full Proposal (RFFP) will be sent to the organization submitting the preproposal. The following is general guidance as to the scope of the proposal for a contract.

The Offeror's proposal shall be submitted in one volume. Two paper copies, of which one is marked "Original" and the remainder "Copy" and an electronic copy of all proposal documents on CD-ROM shall be submitted to the address on page 3 of this BAA. The proposal shall conform to the general formatting guidelines, above. The proposal shall include the following sections, which shall conform to the following page limits:

1. Cover Page (1 page)
 - (a) BAA number

(b) Lead Organization Submitting proposal

(c) Type of business, selected among the following categories: “Large Business,” “Small Disadvantaged Business,” “Other Small Business,” “HBCU,” “MI,” “Other Educational,” or “Other Nonprofit”

(d) Contractor’s reference number (if any)

(e) Proposal Title

(f) Technical point of contact to include: salutation, last name, first name, street address, city, state, zip code, telephone, fax (if available), and electronic mail address (if available)

(g) Administrative point of contact to include: salutation, last name, first name, street address, city, state, zip code, telephone, fax (if available), and electronic mail address (if available)

(h) Date proposal was prepared

2. Technical Section (20 pages)

a) Acronyms, Abbreviations, and Symbols

b) Project objective. Describe what will be accomplished if the U.S. Government funds the proposal. Describe how it fulfills an area of interest described by this BAA.

c) Background data. Include, for example, data supporting the safety and efficacy of the proposed technology, the validity of models used to test and evaluate the technology, and Offeror compliance with GLP, current Good Manufacturing Practices (cGMP), and/or Good Clinical Practices (GCP) compliance, as appropriate.

d) Proposed technical approach. Describe in a comprehensive manner the technical approach proposed to accomplish the project objective. Describe the proposed technical approach in sufficient detail so that the U.S. Government may determine that the proposed approach is of acceptable risk.

3. Project Management Section (20 pages):

a) Statement of Work (SOW). The Offeror shall submit a SOW. The SOW shall describe the work to be performed by the Offeror (and any subcontractors). The final proposed SOW, when accepted by the U.S.

Government, shall be incorporated into the contract or Prototype OT at the time of award. For this reason, the SOW shall be a stand-alone document. Offerors should use the DoD Handbook for Preparation of Statement of Work (MIL-HDB-245D) as a guide found at: <https://assist.daps.dla.mil/quicksearch/>

b) CWBS and CWBS dictionary. The offeror shall submit a CWBS and CWBS dictionary using MIL-HDBK-881 as a guide (http://www.acq.osd.mil/pm/currentpolicy/wbs/MIL_HDBK-881A/MILHDBK881A/WebHelp3/MILHDBK881A.htm). The minimum CWBS expected is Level 4. However, the Offeror shall extend CWBS elements as needed to obtain the depth and breadth required to define the contract scope and to accurately describe the proposed effort. The CWBS shall correlate with the SOW and CLINs. The CWBS shall conform to instructions regarding font size.

c) IMS. The IMS shall document the critical path, major milestones, tasks/activities, duration, lead/lag/slack time, and schedule relationships. The IMS shall be directly traceable to the SOW, CLINs, and the CWBS. The IMS is intended to be used as a tool for day to day tracking of the program/project. Tasks/activities should roll-up to increasingly higher summary levels. All tasks/activities in the IMS should be logically linked together showing predecessor/successor relationships. The tasks/activities shall be sufficient to account for the entire program/project under contract. Dates delineated in the IMS and Section F shall become contractually binding, and will be adjusted accordingly, based on actual contract award date. At the Offeror's option, the IMS may be submitted on large format paper, no greater than 2 meters by 2 meters in size. This will not count against any page limit, other than as needed in the Project Management Section to reference the large-format IMS. The IMS shall conform to instructions regarding font size. The Offeror shall also submit an electronic copy of the schedule for submission of schedule data in "Read Only" format that shows all formulas and links for review. The data file shall be in the native format of the commercially off the shelf software.

d) Project Management Approach. The approach to managing and integrating the various aspects of the required work shall be described in sufficient detail so that the U.S. Government may assess associated risks. The Offeror shall identify significant milestones, decision points, and the processes that will be used to evaluate program status and progress. The Offeror shall include a description of any functional oversight. The Offeror shall present mechanisms for interactions/communications between Program Management and the U.S. Government, to include how processes will be updated (e.g., managing and interfacing with key Subcontractors and the U.S. Government). The Offeror

shall include a description of management relationships or techniques that will be used to supplement day-to-day processes and procedures.

e) Risk Management Plan. The Offeror shall identify potential risks and describe the implementation of an integrated and proactive risk management plan as part of an overall management scheme (e.g., risk planning, risk assessment, risk handling, risk monitoring and documentation). The risk management plan shall discuss integrated methods for identifying, analyzing, prioritizing, and tracking risk drivers and include plans for adequate resources for risk mitigation. The Offeror shall describe tools or methodologies used in the integrated risk management and risk assessment processes.

4. Past Performance Section (10 pages). Information shall be provided for all proposed first-tier subcontractors with whom the Offeror is teaming as well as the Offeror. The Offeror shall list ongoing and previous U.S. Government contracts held during the past three years, which are relevant and demonstrate ability to perform the effort required by the proposal. The Offeror shall explain the relevance of previous efforts with respect to the effort described in the proposal. If the Offeror has limited U.S. Government contracting experience, a description of similar contracts with commercial entities, local and/or state governments should be included, if relevant. Information furnished concerning these efforts shall be similar to that requested of U.S. Government contracts. The Government may send Past Performance questionnaires to Reference(s) listed. For that reason, the offeror must provide current contact information of all references listed in this section, to include: POC name, address, phone number, fax number and email address.

5. Cost Section (40 pages)

The Cost Proposal shall be an integrated and comprehensive estimate with descriptions of estimating techniques and allocation methods that correlate in sufficient depth with the SOO, SOW, CWBS, IMS and CLINs when applicable. Estimating technique(s) used to create the proposal shall be clearly identified. Reasonable and supportable allocation techniques may be used to spread hours and/or cost to lower levels of the CWBS. While it is intended that Offerors shall use their own format for providing the information requested in these instructions, failure to submit all information requested may result in rejection of your proposal. It is highly suggested that the Cost Proposal Spreadsheet be used by Offerors. The Cost Proposal Spreadsheet can be found by following this link: <https://www3.natick.army.mil>. Click on the "proposal spreadsheet" link and save a copy of the spreadsheet. Instructions for completion have been embedded into the spreadsheet. Any proposed options that are identified in the Technical Proposal but are not fully priced out in the Cost Proposal Spreadsheet will not be included in any resulting contract or other transaction. If proposing options, they must be separately priced and separate spreadsheets should be provided for the base period and each option period. For proposed subcontracts, Offerors must provide a separate fully completed Cost

Proposal Spreadsheet in support of the proposed costs. This spreadsheet, along with supporting documentation, must be provided either in a sealed envelope with the prime's proposal or via email directly to the Business Point of Contact at the same time the prime proposal is submitted. The e-mail shall identify the proposal title, the prime Offeror and that the attached proposal is a subcontract. Offerors should also familiarize themselves with the subcontract reporting requirements set forth in Federal Acquisition Regulation (FAR) clause 52.204-10, Reporting Executive Compensation and First-Tier Subcontracts Awards. Any newly awarded subcontract must be reported if the prime contract award amount was \$25,000 or more.

6. Representations, Certifications, and other Statements of Offerors.

Prospective contractors shall complete electronic annual representations and certifications at SAM accessed via <https://www.acquisition.gov> 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.

7. Security Requirements.

Although not to be evaluated, the Offeror shall identify existing or describe capability of obtaining personnel/facilities security clearances.

8. Appendices (no page limit)

9. Key personnel qualifications

10. Other documentation that may be requested by the U.S. Government in the RFFP.

a) Subcontracting Plans (if applicable): Pursuant to Section 8(d) of the Small Business Act (15 U.S.C. 637(d)), it is the policy of the Government to enable small business and small disadvantaged business concerns to be considered fairly as subcontractors to contractors performing work or rendering services as prime contractors or subcontractors under Government contracts, and to ensure that prime contractors and subcontractors carry out this policy. Proposers, other than small businesses seeking an award of greater than \$650,000, who submit a contract proposal and includes subcontractors, are required to submit a subcontracting plan IAW FAR 19.702(a)(1) and (2) and should do so with their proposal. The plan format is outlined in FAR 19.704. As submitted under this BAA, subcontracting plans will be reviewed for adherence to regulations cited in FAR Part 19 and its supplements and not necessarily for evaluation as a specific evaluation criterion. However, an offeror's refusal to submit a subcontracting plan

is grounds for the government to not negotiate award of an offeror's BAA proposal. A sample small business subcontracting plan template is provided at <https://www3.natick.army.mil> under the Broad Agency Announcement webpage.

C. GRANTS

The Federal Financial Assistance Management Improvement Act of 1999, also known as P.L. 106-107, was enacted on November 20, 1999. The purposes of the Act are to (1) improve the effectiveness and performance of Federal financial assistance programs, (2) simplify Federal financial assistance application and reporting requirements, (3) improve the delivery of services to the public, and (4) facilitate greater coordination among those responsible for delivering services.

Grants.gov is an E-Government initiative to provide a simple, unified electronic storefront for interactions between grant applicants and the Federal agencies that manage grant funds. The grant community, including state, local and tribal governments, academia and research institutions, commercial firms and not-for-profits, can access the annual grant funds available across the Federal Government through one website, Grants.gov. In addition to simplifying the grant application process, Grants.gov also creates avenues for consolidation and best practices within each grant-making agency. Further information regarding registering with Grants. Gov is available at: <http://www.grants.gov/web/grants/applicants.html>

In compliance with P.L. 106-107, CBMS JPMO requires proposals submitted for a grant award in response to the BAA to be submitted through Grants.gov. This requires that organizations register in Grants.gov to submit proposals through the Grants.gov portal. Individual Project Managers DO NOT register; however, the Authorized Organizational Representative (AOR) is required to register. The registration process can take several weeks so please register as soon as possible.

Organizations that submit a preproposal or “white paper” and are subsequently invited to submit a full proposal under the BAA may be directed to submit through Grants.gov. Early planning with your organization will facilitate this process. Issues in submitting applications through the Grants.gov portal should be directed to the Grants.gov help desk at 1-800-518-4726 or email support@grants.gov. The Contact Center hours of operation are Monday-Friday, 7 AM to 9 PM Eastern Standard Time.

ii. The following actions are required as part of the registration process. If you do business with the Federal Government on a continuing basis, it is likely you have already completed some of the actions, e.g., obtaining a Data Universal Number System (D-U-N-S®) D-U-N-S® Number. An organization will need a D-U-N-S® Number. A D-U-N-S® Number is a unique nine-character identification number provided by the commercial company Dun & Bradstreet (D&B). If an organization does not have a D-U-N-S®

Number, an authorized official of the organization can request one by calling 1-866-705-5711 Monday-Friday from 7 AM to 8 PM Central Standard Time or online via <http://fedgov.dnb.com/webform>. Organizations located outside of the United States, can request and register for a D-U-N-S® Number online via <http://fedgov.dnb.com/webform>.

iii. SAM. An organization must be registered with the System for Award Management (SAM) before submitting a grant application through Grants.gov or receiving an award from the Federal Government. SAM validates applicant information and electronically shares the secure and encrypted data with federal agencies' finance offices to facilitate paperless payments through Electronic Funds Transfer (EFT). You can register with SAM on line at <https://sam.gov>. If you have the necessary information, online registration will take about 30 minutes to complete, depending upon the size and complexity of your organization, but you should allow 7-10 days after you submit before your registration is active in SAM. Offerors are encouraged to register as soon as possible after receiving this BAA announcement.

1. FULL PROPOSAL PREPARATION FOR GRANTS

a) Mandatory Grant Proposal Forms and Attachments. A complete proposal package includes all required forms and attachments completed, including the full project proposal. The definitive list of required forms is identified at <http://www.grants.gov/> and includes:

1. Standard Form (SF) 424 (Research and Related [R&R]) Application for Federal Assistance.
2. R&R Budget.
3. R&R Subaward Budget Attachment(s) Form (if needed).
4. R&R Project/Performance Site Location(s).
5. R&R Senior/Key Person Profile.
6. R&R Other Project Information. These forms are included in the proposal package.

5. Research Involving Animals. Awards funded by the CBMS JPMO require a second tier review for the use of animals prior to implementation. Therefore, the Project Manager must address all pertinent issues relating to the use of animals in the proposed work effort. Include the required assurances, approvals, forms and description in the proposal addenda entitled "Research Involving Animals," as specified on the Animal Care and Use Review Office (ACURO) website <https://mrmc.amedd.army.mil/rodorpaurd.asp>. Projects performed under CBMS JPMO sponsorship that generate preclinical safety data intended to support a research or marketing permit for products regulated by the FDA must be in conformance with GLP. Full proposals

may be submitted without protocols for animal use; however, protocols and required institution approvals must be submitted not later than 60 days after award to ensure continuation of payments. The contracting office may grant exceptions in situations where animal use is not expected to occur until after the first year of the project. In such cases, a time frame for submission of the appropriate protocols should be established during discussion/negotiations.

D. REGULATIONS AND FORMS

1. The CFR is available at <http://www.gpoaccess.gov/cfr>.
2. The FAR and DFARS are available at website <http://farsite.hill.af.mil>.
3. DoDGARs, DoD 3210.6-R are available at <http://www.dtic.mil/whs/directives/corres/html/32106r.htm>.
4. OMB Circulars are available at <http://www.whitehouse.gov/omb/circulars/index.html>.
5. Representations & Certifications for organizations required to be registered with SAM are available at <https://www.sam.gov>.
6. Additional information on attachments is available at the Grants.gov web portal.

VI. EVALUATION AND SELECTION

A. EVALUATION FACTORS FOR PROCUREMENT CONTRACTS AND GRANTS

Proposals will be evaluated in accordance with the competition requirements of FAR 35.016 (d) and (e), or 10 USC 2361, 10 USC 2371, 10 USC 2374, or DoDGARs 3210.6-R as appropriate. Specifically:

Proposals received as a result of the BAA shall be evaluated in accordance with evaluation criteria specified therein through a peer or scientific review process. Written evaluation reports on individual proposals will be necessary but proposals need not be evaluated against each other since they are not submitted in accordance with a common work statement.

The primary basis for selecting proposals for acceptance shall be technical, importance to agency programs, and fund availability. Cost realism and reasonableness shall also be considered to the extent appropriate.

Full proposals will be evaluated by JPM MCS scientists, other Federal Agency Representatives, outside scientists with diverse expertise, clinicians, consumers, or combinations thereof will

evaluate proposals and assign scores based on the following factors (in descending order of importance):

1. Technical Merit: The proposed plans, methods, techniques, and procedures must be feasible, clear, valid, adequately referenced, and state-of-the-art. The proposed schedule must be reasonable. Literature searches are recommended for documenting the strengths of the proposed project.

2. Military and Program Relevance: Projects must support the development of medical CBRN countermeasures, to include Countermeasure Prototypes, Special Projects, and Developmental Initiatives Supporting Medical CBRN Countermeasures and Enabling Technologies, as described in the “Areas of Interest” portion of this BAA and subsequent amendments. Proposals should address an outstanding requirement and balance or reduce programmatic risk of the current JPM MCS medical CBRN countermeasure development program. Explain how the results of this project are expected to impact the intended beneficiaries.

3. Funds Availability: JPM MCS must have funds available to support the proposed work.

4. Technology Readiness Level (TRL): JPM MCS does not fund basic, applied, or advanced research. The technology proposed must meet TRL 4. See the attached for a full description of TRLs (Q-TRLS).

5. Project Objectives: The stated objectives must be clear, valid and logical. Projects that demonstrate an innovative approach are desired.

6. Regulatory compliance. The proposal will be evaluated for compliance with FDA guidelines for current cGMP, GLP, and GCP.

7. Support of other U.S. Government requirements. The proposal will be evaluated for alignment with other DoD requirements and the medical CBRN Medical Countermeasure development efforts of the Department of Health and Human Services, the Department of Veterans Affairs, or the Department of Homeland Security.

8. Key Personnel Qualifications: Document the qualifications, capabilities and experience of the proposed Project Manager and other key personnel in sufficient details to demonstrate that the proposed staff has the knowledge and skills to achieve the proposed objectives.

9. Facilities: Describe the proposed facilities and equipment, or unique combinations of these, in detail to demonstrate that the organization has the necessary facilities required for the accomplishing the proposed objectives.

10. Budget/Cost: The budget must reflect the actual needs of the proposed work and be fully justified so that the U.S. Government can evaluate and determine the cost to be fair and reasonable and commensurate with the complexity and nature of the work proposed. Where applicable, comparative cost will be employed as determined by JPM MCS in its discretion.

11. Past Performance: Documented satisfactory performance record. In the case of an offeror without a record of relevant past performance or for whom information on past performance is not available, the offeror may not be evaluated favorably or unfavorably on past performance.

B. SELECTION FOR PROCUREMENT CONTRACTS AND GRANTS

Any proposal received may be negotiated. After the JPM MCS evaluation, proposals recommended for funding will be prioritized. A prioritized listing of alternates may also be prepared when warranted. Subsequent awards depend upon the availability of funds and fulfillment of requirements and priorities determined to exist at the time of award. In some cases, funding priorities may change as certain scientific tasks are addressed and new mission assignments arise. Award may also be dependent upon demonstration by the applicant that they have adequately addressed the following requirements, if applicable to the efforts being proposed:

1. Research involving Human Subjects/Anatomical Substances (if proposed).
2. Research involving Animals (if proposed).
3. Facility Safety Plan.
4. Certificate of Environmental Compliance.
5. Evidence of GLP Compliance (if appropriate).
6. Evidence of cGMP Compliance (if appropriate).
7. Evidence of GCP Compliance (if appropriate).
8. All required Representations and Certifications are completed and on file.

VII. AWARD ADMINISTRATION

A. PAYMENT

1. CONTRACTS

In accordance with DFARS Clause 252.232-7003, Electronic Submission of Payment Requests, the contractor shall submit invoices electronically. Invoices shall be made using the DoD's

Wide Area Workflow (WAWF) system, Web Invoicing System, or system acceptable to the contracting or agreements officer. Information about WAWF can be found at <https://wawf.eb.mil/>. Contractors must be able to electronically receive payment funds.

2. GRANTS

Recipients of cost-reimbursable grants must request payment using SF 270. Grants may also include scheduled payments if warranted. Grant recipients must be able to electronically receive funds in accordance with DoDGARs 22.810.

B. INFORMATION RELEASE

JPM MCS must approve the release of information pertaining to projects funded by JPM MCS. Approval must be sought through the cognizant Contracting, Grants, or Agreements Officer. Statement 1 shall be included in all such information releases; Statements 2-6 shall be included if relevant to the work being conducted.

1. “This work was supported by the Joint Project Manager Medical Countermeasure Systems under the Army Contracting Command – Aberdeen Proving Ground – Natick Contracting Division – Ft. Detrick, Award No. _____. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.”

2. In conducting research using humans and/or human anatomical substances, the investigator is required to include approvals, forms and information specified on the HRPO website:
https://mrmc.amedd.army.mil/index.cfm?pageid=research_protections.hrpo

3. “In conducting research using animals, the investigator(s) adheres to the laws of the United States and regulations of the Department of Agriculture.” Include required assurances, approvals, forms and information specified on the ACURO website
https://mrmc.amedd.army.mil/index.cfm?pageid=research_protections.acuro

4. “In the conduct of research utilizing recombinant DNA, the investigator adhered to National Institutes of Health (NIH) Guidelines for research involving recombinant DNA molecules.” (<http://www.nih.gov>)

5. “In the conduct of research involving hazardous organisms, the investigator adhered to the Centers for Disease Control (CDC)-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.”
(<http://www.cdc.gov/od/ohs/biosfty/biosfty.htm>)

6. “Information” includes, but is not limited to, news releases, articles, manuscripts, brochures, advertisements, still and motion pictures, speeches, trade

association meetings, and presentations or posters at scientific conferences, workshops, and symposia.

C. FREEDOM OF INFORMATION ACT REQUESTS

The FOIA (5 USC 552) provides a statutory basis for public access to official U.S. Government records. "Records" are defined to include documentation received by the U.S. Government in connection with the transaction of public business. Records must be made available to any person requesting them unless the records fall under one of nine exceptions to the Act <http://www.usdoj.gov/oip>.

When a FOIA request asks for information contained in a successful proposal that has been incorporated into an award document, the submitter will be contacted and given an opportunity to object to the release of all or part of the information that was incorporated. A valid legal basis must accompany each objection to release. Each objection will be evaluated by ACC-APG Natick in making its final determination concerning which information is or is not releasable. If information requested is releasable, the submitter will be given notice of ACC-APG Natick's intent to release and will be provided a reasonable opportunity to assert available action.

D. SITE VISITS

JPM MCS personnel may visit the award recipients during the project. All visits shall be coordinated with the cognizant Contracting, Grants, or Agreements Officer and are intended for technical discussion and monitoring of progress of the funded project.

E. REPORTS/MEETINGS/KNOWLEDGE DISEMINATION

Reports are necessary for continuation of funding. Reporting requirements are determined by the Contracting, Grants, or Agreements officer and reflect the type of award (grant, procurement contract; firm fixed price or cost-reimbursable). Each request for full proposal will state the necessary reports that will be required. The Offeror must price all reports and deliverables. Reporting requirements may include the following:

1. Monthly or quarterly reports that outline the accomplishments and progress for that period.
2. Quarterly In-Process Reviews to discuss findings, accomplishments and direction for the program.
3. SF 272, Federal Cash Transaction Report, filed quarterly when grants with scheduled payments are made.
4. SF 269, Financial Status Report. Required for grants either annually or at project termination.
5. Annual reports that consist of detailed summaries of scientific issues, accomplishments and animal research usage during the project.

- 6. Final report that details the findings and issues of the completed project.
- 7. Disclosure of subject inventions in accordance with 37 CFR 401 using DD Form 882.
- 8. Copies of all scientific publications as a result of funding.
- 9. Abstracts suitable for publication in relation to planned meetings.
- 10. A Program Review shall be held annually at the Government’s site in which the Recipient will be required to provide briefing charts and an oral presentation on their efforts achieved as a result of Government awarded funding.

F. AUDITS AND COST PRINCIPLES

Organizations receiving grants and cost-reimbursable contracts must be audited. See below for the governing cost principles for each award/business type.

1. Cost-Reimbursable Contracts

The Contractor’s accounting system must be approved by the cognizant Administrative Contracting Officer (ACO). The following cost principles apply:

Organization Type	Cost Principles
Educational Institutions	FAR 31.3
Nonprofit institutions	FAR 31.7
For-profit institutions	FAR 31.2 and DFARS part 231

2. Grants

Recipients are to periodically have independent financial and compliance audits subject to DoDGARs 32.26. The following cost principles apply:

Organization Type	Cost Principles
Educational Institutions	2 CFR Part 220 (formerly OMB Circular A-21)
Nonprofit institutions	2 CFR Part 230 (formerly OMB Circular A-122)
For-profit institutions	FAR 31.2 and DFARS part 231

VIII. JPM MCS MISSION STATEMENTS AND AREAS OF INTEREST

A. SCOPE OF PROPOSALS SOUGHT

JPM - MCS is interested in proposals that are based on data from experiments using specific CBRN warfare agents, not surrogates, to demonstrate safety, efficacy or mode of action. (Please note that CBRN warfare agents will not be provided by the DoD for these efforts.) We are interested in studies on new and better ways to develop medical CBRN countermeasures more rapidly and with increased efficiency through enabling technologies, life cycle bioinformatics, and improved logistics tracking. We are not interested in proof-of-concept, advanced, applied or basic research proposals. We are interested in efforts directed toward the development of enabling technologies that speed up the advanced development process leading to FDA approval. All developmental efforts nominated to be considered by this BAA should be evaluated against the Quality Technology Readiness Levels (Q-TRL) for Medical Product Development (Appendix A). Potential developmental efforts must be consistent with the minimum criteria at TRL level 4 for transition to advanced development. In particular, the scope of work proposed under this BAA must be limited to TRL 4 levels described at 4-M1, 4-D1 and 4-E1 for Medical Products and 4-DAM1, 4-DAS1 and 4-DCS1 for Diagnostics (see attached Q-TRL List)

B. DEFINITIONS

Development. The systematic use of scientific and technical knowledge in the design, development, testing, or evaluation of potential new products, processes, or services to meet specific performance requirements or objectives. It includes the functions of design engineering, prototyping, and engineering testing. Advanced development consists of activities that plan, produce and deliver information outputs (documents, data, and records) from discovery all the way through Phase 4 post-marketing studies and surveillance. The general phases of the lifecycle are discovery, preclinical, and clinical phases.

Enabling Technologies. Technologies that are not countermeasure products or systems themselves but facilitate or accelerate the development of countermeasure products or systems. Examples of enabling technologies include combinatorial chemistry, high-throughput screening, microarrays, bioinformatics and computational biology, nanotechnologies, imaging (including biosensors and biomarkers), animal models, assays, and other product development tools.

Health Surveillance. The ongoing, systematic collection, analysis, and interpretation of health-related data to detect and assess CBRN warfare risks in order to plan, implement, and evaluate prevention and intervention/response programs. Included are computational models, such as expert systems and predictive models.

Improved Logistics Tracking. Technologies which facilitate tracking and monitoring individual product items throughout shipping, storage, delivery to, and use by the end user (factory to foxhole). Examples include technologies which facilitate or simplify supply chain management and/or shelf life extension, such as Time Temperature Indicators (TTI), Item Unique Identification (IUID), and Radio-Frequency Identification (RFID).

Joint Project Manager (JPM). The designated individual with responsibility for and authority to accomplish program objectives for development, production, and sustainment to meet the user's operational needs. The JPM is accountable for credible cost, schedule, and performance reporting to the Milestone Decision Authority (MDA).

Life Cycle Bioinformatics. The systematic collection and analysis of data from all phases of research, development, manufacturing, and test and evaluation to enable informed decision making. Included are data obtained from preclinical studies, ensuring compliance with 21 Code of Federal Regulations (CFR) part 11.

Milestone Decision Authority (MDA) (JPEO-CBD). The designated individual with overall responsibility for the Chemical and Biological Defense Program. The MDA has the authority to approve entry of an acquisition program into the next phase of the acquisition process and shall be accountable for cost, schedule, and performance reporting to higher authority, including Congressional reporting.

C. MEDICAL COUNTERMEASURES SYSTEM JOINT DEPUTY PRODUCT MANAGERS, ORGANIZATIONAL MISSION STATEMENTS AND BAA TECHNICAL POINTS OF CONTACT

1. Joint Vaccine Acquisition Program (JVAP): Develop, produce & stockpile FDA-licensed vaccine systems to protect the Warfighter from biological agents.

JVAP Technical POC: Dr. David Hone
Email: david.m.hone.ctr@us.army.mil

2. Chemical Defense Pharmaceuticals (CDP): Provide the Warfighter and the Nation robust & affordable FDA-approved lifesaving medical countermeasure drug capabilities against chemical, biological, radiological and nuclear threats.

CDP Technical POC: Dr. Renae Malek (CBMS JPMO)
Email: renae.malek@amedd.army.mil

3. Biological Defense Therapeutics (BD TX): Provide US military forces and the nation safe, effective, innovative, and affordable therapeutic solutions to counter traditional, emerging and engineered biological threats.

BD TX Technical POC: Dr. George Christopher (TMT JPMO)
Email: George.christopher@dtra.mil

4. Diagnostics: Develop and integrate chemical, biological, radiological & nuclear (CBRN) technologies to enable early warning, identification, and continued situational awareness of potential global health threats.

Diagnostics Technical POC: Jason Opdyke

Email: Jason.opdyke.ctr@mail.mil

5. Critical Reagents Program (CRP): To serve as the principal resource of high quality, validate, and standardized biological detection assays and reagents that meet the requirements of the Warfighter and joint biological defense systems and support the biological defense community by facilitating the transition of new technologies and coordinating their advanced development, efficient production, and timely distribution.

CRP Technical POC: Dr. Michael Smith, CRP Director

Email: Michael.aaron.smith1@us.army.mil

6. Advanced Development & Manufacturing capabilities (ADM_c): Develop a national capability and capacity to develop and produce MCMs rapidly to counter known or unknown CBRN threats, including novel and previously unrecognized, naturally-occurring emerging infectious diseases.

ADM_c Technical POC: Dr. Christopher Earnhart, Acting Director, Medical Countermeasure Integration

Email: christopher.earnhart@navy.mil

D. MISSION AREAS

1. MEDICAL BIOLOGICAL PROPHYLAXIS

Biological Medical Prophylaxis provides medical countermeasures against biological warfare agents. These countermeasures include specialized medical materiel (e.g., vaccines and immunotherapeutics) as well as other biological products (e.g., immunoglobulins) designed to be effective as prophylaxis or, to treat rare but serious adverse events from other prophylaxis treatments. Biological Medical Prophylaxis countermeasures must be FDA-approved to provide the Joint Force with the ability to protect Warfighters from the debilitating and life threatening health threats of biological warfare agents (bacteria, viruses, and biotoxins) prior to the appearance of symptoms, thereby protecting Warfighters, conserving the strength of forces, and reducing the impact on the medical care system.

Biological Medical Prophylaxis countermeasures should protect against battlespace challenge of biological warfare agents (BWA) (e.g., aerosol exposure), be deliverable by minimally invasive

means in as few doses as feasible, provide protection as quickly as possible, maintain protection as long as possible, be effective against a broad spectrum of agents, and be flexible enough to respond to a wide range of agents, including genetically altered agents. Biological Medical Prophylaxis countermeasures should limit the logistic burden on the force through limited special storage or handling requirements, reduced dosing, administration, and monitoring requirements. These capabilities must also provide for insertion of technology upgrades and commonality of components to address changing threats.

Overarching priorities of the Biological Medical Prophylaxis program include:

1. Develop prophylaxis or pretreatment systems to protect Warfighters from the effects of biological warfare agents prior to the appearance of symptoms. Primary prevention through vaccination is generally preferred as a long term goal, where possible and supported by the nature of the agent. Vaccine development is historically a difficult, expensive, and time-consuming effort. Vaccines are agent, and frequently subtype specific. For these reasons, there is particular interest in broad spectrum protection and multi-agent medical products.

- a. Vaccine development which focuses on protection from agents in aerosol exposure, molecular approaches for development of vaccines, measurement of relevant cellular and humoral protective immune responses, and expression or production of protective antigens using recombinant technology.

- b. Vaccine development for specific toxins and disease agents which could involve the generation, selection and characterization of attenuated strains or inactivated purified antigen preparations, to include polyvalent vaccines that are more broadly effective.

- c. Safer means of passive immunization, such as production of human monoclonal or modified antibodies that are despeciated.

2. Prevention, treatment, or supportive care regimens for adverse reactions to prophylaxis or pretreatments. Some vaccines or other pretreatments occasionally result in adverse reactions that require treatment themselves, such as in the case of smallpox vaccine. In such circumstances, an immune globulin or other biological or drug product is required to be part of the vaccine or product “system” to prevent or treat rare but potentially serious adverse events. FDA approval is required for these associated products.

3. Enabling technologies that support, facilitate, or accelerate the development or licensure of Biological Medical Prophylaxis countermeasures.

a. Identification of correlates of protection for the agents described above and development of assays to assess such protection.

b. Development/characterization of relevant animal models to meet FDA licensing requirements for biodefense biologics.

c. Development of improved methods for delivery of vaccines, including adjuvants, nucleic acid vaccines, methods for oral or nasal immunization with inactivated, live and subunit antigens; sustained release formulations; and methods for delivery of antigens for specific induction of mucosal immunity and development of methods to enhance appropriate immune responses to include co-delivery of cytokines.

d. Development of improved methods to characterize vaccine products, including potency, identity, and purity.

e. Development of single use system (SUS) manufacturing technologies and processes to facilitate transition and future production of MCM.

4. Infectious agents upon which the Biological Medical Prophylaxis program places its current focus include Ebola virus, Marburg virus, poxvirus models of variola virus and those agents causing Venezuelan equine encephalitis, western and eastern equine encephalitis, Tularemia, Plague, Q-fever, and Brucellosis. Toxins of interest include those from plants (ricin), bacteria (Staphylococcal enterotoxins, botulinum toxin serotypes A, B, C, D, E, F, G), and membrane damaging toxins.

2. MEDICAL CHEMICAL AND BIOLOGICAL COUNTERMEASURES

Prophylactic/pretreatment and therapeutic pharmaceuticals are non-vaccine pharmacological or biological products used to prevent or treat patients exposed to either chemical warfare agents (CWA) or biological warfare agents (BWA). Therapeutic pharmaceuticals could be administered pre- or post-exposure. The products are of the type that are to be licensed or approved by the FDA for their intended use, potentially to include juvenile, geriatric, or immunocompromised patients. Treatment of chemical and biological casualties depends on effective use of multiple medical capabilities in an integrated manner. Warfighters may use self-administered pharmaceuticals or may administer pharmaceuticals to another Warfighter. Health care providers must have appropriate pharmaceuticals, tools to diagnose and monitor response of casualties, and appropriate means to protect themselves from chemical and biological hazards. We are particularly interested in developing medical countermeasures that are active against a broad spectrum of chemical or biological agents. Chemical agents of concern fall under the broad categories of nerve, blister, blood, and pulmonary agents. Biological agents of concern

include bacterial, toxin and viral threat agents. Bacterial warfare threat agents of interest include *Bacillus anthracis*, *Yersinia pestis*, *Francisella tularensis*, *Burkholderia pseudomallei*, and *Burkholderia mallei*, to include emerging, genetically altered, and multi-drug resistant strains. Toxin threat agents of interest include Botulinum Neurotoxin (BoNT), Ricin, and Staphylococcal Enterotoxins (SE). Viral threat agents of interest include Alphaviruses (i.e., Venezuelan Equine Encephalitis virus [VEE], Western Equine Encephalitis virus [WEE] and Eastern Equine Encephalitis virus [EEE]), Orthopoxvirus (i.e., Variola and Monkeypox), Filoviruses (i.e. Ebola virus and Marburgvirus), Arenaviruses (Junin virus and Lassa virus), Bunyaviruses (Hantaan virus and Rift Valley Fever virus),. Of interest is science focusing on characterizing the nature of the threat to identify key targets for intervention or disruption of the agents and their effects. Gene or nucleotide therapeutics and protein-based therapeutics targets are identified as promising areas/products for investment by DoD. Metabolomics technology is also identified as a way to discover and develop new countermeasures against biological warfare threats.

Overarching goals of the Medical Chemical and Biological Countermeasures projects include:

1. Develop systems that support maintenance or restoration of pre-CWA or pre-BWA exposure health and that allow Warfighters to complete their mission. This includes medical CWA or BWA countermeasures that prevent, reverse, or significantly mitigate the effects and negative operational impact of CWA or BWA. Medical countermeasures may block, stop or reverse the direct effects of these agents, or prevent or treat the pathology and symptoms of these agents.
2. Develop medical countermeasures that provide broad-spectrum prevention or treatment for classes of chemical or biological agents and a range of exposure routes. Threats from chemical agents are likely to become more complex in the future as a result of increased agent variety and sophistication. The effects of biological agents are likely to be more difficult to mitigate as a result of genetic engineering and the natural evolution of multidrug resistance. Therefore, the products should be flexible enough to respond to a wide range of warfare agents, including traditional and emerging agents. Medical CWA countermeasure systems might also include developing therapies and protocols for treatment that mitigate agent persistence or special effects of new threat agents, such as those that can potentially penetrate protective clothing.
3. Evaluate and leverage enabling technologies to enhance/prolong the shelf life of nerve agent countermeasures currently in the military arsenal. Areas of focus include developing new container-closure systems, wet-dry autoinjectors or formulation development.

3. MEDICAL RADIOLOGICAL COUNTERMEASURES

The goal of the Medical Radiological Countermeasures (MRADC) projects are to select, develop, and manufacture FDA-approved drugs, biologics and diagnostics (e.g., biodosimetry) to increase survival and decrease incapacity by treating or detecting the incipient or manifest radiation injury following exposure to radiation from nuclear or radiological weapons so that Warfighters can maintain operational effectiveness. MRADC must be safe, efficacious, free of performance-degrading side effects, compatible with current military CBRN countermeasures, and usable while in combat or garrison, during medical evacuation, and in hospital. Desired, but not mandatory, product attributes include ease of administration (e.g., autoinjector) and administrable to subjects wearing military protective gear, efficacy with a single dose or short course of treatment, and retained efficacy even if delivered more than four hours after radiation exposure. MRADC should not require refrigeration or have other significant logistical burdens and should have a relatively long shelf life. Excluded from consideration under this BAA are candidate MRADC next generation antibiotics and probiotics, blocking, decorporation, and purgative agents, blood (or blood component) replacements or substitutes, antiemetics and other comfort or supportive measures.

4. MEDICAL DIAGNOSTIC AND SURVEILLANCE SYSTEMS

The DoD has a need for technologies for the prediction, detection, identification, and clinical diagnosis of infection by warfare pathogens and toxins. Sensitivity, specificity, ease of use, and deployability (size, weight, power requirements, reduced consumables) are critical features of such systems. An integrated system using multiple technology approaches that will reduce the potential for misdiagnosis of a BWA or other disease agent in clinical samples will provide the solution for future diagnostic capabilities. CBMS JPMO is interested in developmental efforts that improve the ability of DoD entities to perform identification and characterization of infectious disease and biological warfare threat agents associated with veterinary, arthropod vector, and environmental surveillance samples.

5. CRITICAL REAGENTS PROGRAM (CRP)

The CRPs mission is to serve as the principal resource of high quality, validated, and standardized biological detection assays and reagents that meet the requirements of the Warfighter and Joint biological defense systems. CRP products include antibodies, inactivated antigens, genomic materials, electrochemiluminescence (ECL) assays, polymerase chain reaction assays (PCR), lateral flow immunoassays (LFI).

The CRP seeks to support the biological defense community by facilitating the transition of new technologies and coordinating their advanced development, efficient production and timely distribution. The goal of the CRP is to be recognized as the provider of choice for a

comprehensive portfolio of world-class biological detection assays and reagents to safeguard the warfighter and for warfare defense.

IX. ATTACHMENTS AND APPENDICES

Appendix 1. Application Submission and Receipt Procedures for Grants.Gov

This section provides the application submission and receipt instructions for program applications. Please read the following instructions carefully and completely.

1. Electronic Delivery. Grants.gov is an initiative that provides the Grant Community a single site to find and apply for grant funding opportunities. Applicants are encouraged to submit their applications electronically through <http://www.grants.gov/web/grants/applicants/apply-for-grants.html>.

2. The following describes what to expect when applying online using Grants.gov/Apply:

a. Instructions. On the site, you will find step-by-step instructions which enable you to apply for funds. The Grants.gov/Apply feature includes a simple, unified application process that makes it possible for applicants to apply for grants online. There are five "Get Registered" steps for an Organization to complete at Grants.gov. The information applicants need to understand and execute the steps can be found at <http://www.grants.gov/web/grants/applicants/organization-registration.html>.

Applicants should read through the registration process carefully. The site also contains registration checklists to help you walk through the process. Applicants are recommended to download the checklists and prepare the information requested before beginning the registration process. Reviewing and assembling required information before beginning the registration process will alleviate last minute searches for required information and save time.

b. DUNS Requirement. All applicants applying for funding, including renewal funding, must have a Dun and Bradstreet Universal Data Numbering System (DUNS) number. The DUNS number must be included in the data entry field labeled "Organizational DUNS" on the SF-424 form. Instructions for obtaining a DUNS number can be found at the following website: <http://www.grants.gov/web/grants/applicants/organization-registration/step-1-obtain-duns-number.html>.

c. System for Award Management. In addition to having a DUNS number, applicants applying electronically through Grants.gov must register with the federal System for Award Management (SAM). Step-by-step instructions for registering with SAM can be found here: <http://www.grants.gov/web/grants/applicants/organization-registration/step-2-register-with-sam.html>. All applicants must register with SAM in order to apply online. Failure to register with the SAM will result in your application being rejected by Grants.gov during the submissions process.

d. Username and Password. The next step in the registration process is creating a username and password with Grants.gov to become an Authorized Organizational Representative (AOR). AORs will need to know the DUNS number of the organization for which they will be submitting applications to complete this process. To read more detailed instructions for creating a profile on Grants.gov visit: <http://www.grants.gov/web/grants/applicants/organization-registration/step-3-username-password.html>.

e. AOR Authorization. After creating a profile on Grants.gov, the E-Biz Point of Contact (E-Biz POC) a representative from your organization who is the contact listed for SAM will receive an email to grant the AOR permission to submit applications on behalf of their organization. The E-Biz POC will then log in to Grants.gov and approves an applicant as the AOR, thereby giving him or her permission to submit applications. To learn more about AOR Authorization visit: <http://www.grants.gov/web/grants/applicants/organization-registration/step-4-aor->

[authorization.html](http://www.grants.gov/web/grants/applicants/organization-registration/step-5-track-aor-status.html). To track an AOR status visit: <http://www.grants.gov/web/grants/applicants/organization-registration/step-5-track-aor-status.html>.

Applicants are, therefore, encouraged to register early. The registration process can take up to four weeks to be completed. Therefore, registration should be done in sufficient time to ensure it does not impact your ability to meet required submission deadlines. You will be able to submit your application online anytime after you have been approved as an AOR.

f. Electronic Signature. Applications submitted through Grants.gov constitute a submission as electronically signed applications. The registration and account creation with Grants.gov with E-Biz POC approval, establishes an Authorized Organization Representative (AOR). When you submit the application through Grants.gov, the name of your AOR on file will be inserted into the signature line of the application. Applicants must register the individual who is able to make legally binding commitments for the applicant organization as the Authorized Organization Representative (AOR); this step is often missed and it is crucial for valid submissions.

3. Instructions on how to submit an electronic application via Grants.gov/Apply:

Grants.gov has a full set of instructions on how to apply for opportunities on its website at <http://www.grants.gov/web/grants/applicants/grant-application-process.html>. The following provides simple guidance on what you will find on the Grants.gov/Apply site. Applicants are encouraged to read through the page entitled, "Complete Application Package" before getting started.

Grants.gov allows applicants to download the application package, instructions and forms that are incorporated in the instructions, and work offline. In addition to forms that are part of the application instructions, there will be a series of electronic forms that are provided utilizing Adobe Reader.

a. Adobe Reader. Adobe Reader is available for free to download from on the Download Software page: <http://www.grants.gov/web/grants/support/technical-support/recommended-software.html>. Adobe Reader allows applicants to read the electronic files in a form format so that they will look like any other Standard form. The Adobe Reader forms have content sensitive help. This engages the content sensitive help for each field you will need to complete on the form. The Adobe Reader forms can be downloaded and saved on your hard drive, network drive(s), or CDs.

NOTE: for the Adobe Reader, Grants.gov is compatible with versions 8.1.1 and later versions. Always refer to the Download Software page for compatible versions. Please do not use lower versions of the Adobe Reader.

b. Mandatory Fields in Adobe Forms. In the Adobe Reader forms you will note fields that will appear with a background color on the data fields to be completed. These fields are mandatory fields and they must be completed to successfully submit your application.

c. Completion of SF-424 Fields First. The Adobe Reader forms are designed to fill in common required fields such as the applicant name and address, DUNS number, etc., on all Adobe Reader forms. To trigger this feature, an applicant must complete the SF-424 information first. Once it is completed the information will transfer to the other forms.

d. Customer Support. The Grants.gov website provides customer support via toll-free 1-(800)-518-GRANTS or through email at support@grants.gov. For grant opportunity related questions, contact the number listed in the application package of the grant you are applying for. If you are experiencing difficulties with your submission it is

best to call the Contact Center and get a case number. The case number will assist the [INSERT AGENCY NAME] with tracking your issue and provide background information on the issue.

4. Timely Receipt Requirements and Proof of Timely Submission.

a. Electronic Submission. All applications must be received by the Eastern time on the due date established for each program (if applicable). Proof of timely submission is automatically recorded by Grants.gov. An electronic time stamp is generated within the system when the application is successfully received by Grants.gov. The applicant will receive an acknowledgement of receipt and a tracking number from Grants.gov with the successful transmission of their application. Applicants should print this receipt and save it, along with facsimile receipts for information provided by facsimile, as proof of timely submission. When the agency successfully retrieves the application from Grants.gov, Grants.gov will provide an electronic acknowledgment of receipt to the email address of the AOR. Proof of timely submission shall be the date and time that Grants.gov receives your application. Applications received by Grants.gov, after the established due date for the program will be considered late and will not be considered for funding.

Applicants using dial-up connections should be aware that transmission should take some time before Grants.gov receives it. Grants.gov will provide either an error or a successfully received transmission message. The Grants.gov Contact Center reports that some applicants abort the transmission because they think that nothing is occurring during the transmission process. Please be patient and give the system time to process the application. Uploading and transmitting many files particularly electronic forms with associated XML schemas will take some time to be processed.



Harmonized Q-TRL List for Medical MCMs

The US Department of Health and Human Services (HHS) and the Department of Defense (DoD) are engaged in the development of medical countermeasures (MCM) for Chemical, Biological, Radiological and Nuclear (CBRN) threats. The DoD and HHS utilize harmonized Technology Readiness Levels (TRLs) as a common method to understand at a general level the maturity of MCM development products in development across the USG. TRLs consist of nine progressive levels of milestones over a product development lifecycle.

Quantitative Technological Readiness Levels (Q-TRLs) expand the nine high-level TRLs to a much more detailed level to provide key development milestones and activities specific to vaccine, small molecule, biologics and diagnostics. These Q-TRLs are not intended to be a requirement for each project but rather to provide a selection of milestones and activities throughout the development lifecycle from discovery through post-approval.

Naming Conventions

For the Q-TRL naming conventions the first number denotes TRL level, second letter denotes functional areas, last number is sequential number of Q-TRL in a functional area. For Medical MCMs the letter R is Regulatory, C is clinical, D is non-clinical development, E is non-clinical efficacy and M is CMC.



Q-TRL List			
TRL Level	Sub Level	Product Development Area	Q-TRL Description
1		Overview	Review of Scientific Knowledge Base. Active monitoring of scientific knowledge base to identify countermeasure candidates. Scientific findings are reviewed and assessed as a foundation for characterizing approaches to intervene in disease.
	1-R1	Regulatory	No Activity.
	1-M1	CMC	Establish consultant contacts with target/candidate experts (if applicable)
	1-D1	Non-Clinical Development	No Activity.
	1-E1	Non-Clinical Efficacy	Identify threat agent challenge agent and make link.
	1-E2		Perform natural/case history studies of threat agent.
	1-E3		Pathogenesis, and pathophysiology studies to relate to humans.
	1-C1	Clinical	Review the pathology of human disease.
2		Overview	Development of Hypotheses and Experimental Designs Develop research ideas, hypotheses, and experimental designs for addressing the related scientific issues. Focus on practical applications based on basic principles. Use of computer simulation or other virtual platforms to test hypotheses may be used.
	2-R1	Regulatory	No Activity.
	2-M1	CMC	Review scientific literature, and design theoretical synthesis processes that may be evaluated in the laboratory to yield the selected bulk drug substance (BDS) candidate.
	2-D1	Non-Clinical Development	No Activity.
	2-E1	Non-Clinical Efficacy	Identify and characterize threat agent.
	2-E2		Generate hypotheses for types of animal models.
	2-E3		Perform exploratory studies.
	2-E4		Summarize the description of the human disease.
	2-C1	Clinical	No Activity.
3		Overview	Target/Candidate Identification and Characterization of Preliminary Candidates(s) Begin research, data collection, and analysis in order to test hypothesis. Explore alternative concepts, identify and evaluate critical technologies and components, and begin characterization of candidate(s). Preliminary efficacy demonstrated in vivo. 3A Identify target and/or candidate. 3B Demonstrate in vitro activity of candidate(s) to counteract the effects of the threat agent. 3C Generate preliminary in vivo proof-of-concept efficacy data (non-GLP[Good Laboratory Practice])
	3-R1	Regulatory	No Activity.
	3-M1	CMC	Perform laboratory scale experiments to test feasibility of lab scale manufacturing



Q-TRL List

TRL Level	Sub Level	Product Development Area	Q-TRL Description
			hypothesis. Explore alternative synthesis/manufacturing approaches to enhance yield and purity and document processes.
	3-M2		Identify the candidate or prototypes
	3-M3		Lab-scale production of candidate product.
	3-M4		Formulate an experimental drug product (EDP) for preliminary animal studies.
	3-M5		Initiate development of appropriate and relevant preliminary assays to evaluate lab-scale product
	3-M6		Establish reference materials with document histories
	3-M7		Complete Research tech transfer report
	3-M8		Complete tech transfer from Research to Development
	3-D1	Non-Clinical Development	Conduct in-vitro testing to determine pre-clinical baseline (Therapeutic Index e.g. MIC, ED50, including in-vitro safety: genotoxicity)
	3-E1	Non-Clinical Efficacy	Select type strain candidate(s) or physical/physiochemical forms of challenge agent.
	3-E2		Complete pathology studies of the animals that were exposed to the challenge agent.
	3-E3		Identify facilities for physical agent exposure.
	3-E4		Complete dose ranging with challenge agent, monitoring clinical endpoints (non-invasive).
	3-E5		Determine the mechanism of action through pathogenesis & exploratory studies.
	3-E6		Identify critical parameters and outcomes in probable animal models.
	3-E7		Conduct initial proof-of-concept animal efficacy studies in one probable animal model (small animals are acceptable).
	3-C1	Clinical	No Activity.
4		Overview	Candidate Optimization and Non-GLP In Vivo Demonstration of Activity and Efficacy Initiation of animal model development. Non-GLP in vivo toxicity and efficacy demonstration in accordance with the product's intended use. Initiation of experiments to identify markers, correlates of protection, assays, and endpoints for further non-clinical and clinical studies. 4A Demonstrate non-GLP in vivo activity and potential for efficacy consistent with the product's intended use (i.e. dose, schedule, duration, route of administration, and route of threat agent challenge) 4B Conduct initial non-GLP toxicity studies and determine pharmacodynamics and pharmacokinetics and/or immune response in appropriate animal models (as applicable) " 4C Initiate experiments to determine assays, parameters, surrogate markers, correlates of protections, and endpoints to be used during non-clinical and clinical studies to further evaluate and characterize candidate(s).
	4-R1	Regulatory	Request and conduct pre-pre-IND meeting, if necessary including discussions of the concept for animal models



Q-TRL List

TRL Level	Sub Level	Product Development Area	Q-TRL Description
	4-M1	CMC	Demonstrate Capability to Produce the Technology in a Lab Environment. Prepare laboratory-scale non-GLP/non-cGMP quantities of BDS to further refine manufacturing process. Formulate an experimental drug product (EDP) for preliminary animal studies. Evaluate BDS and EDP for conformance to preliminary specifications.
	4-M2		Conduct physical-chemical characterization of BDS.
	4-M3		Expand on preliminary development of appropriate and relevant assays and associated reference standards/reagents for the desired formulations. Demonstrate suitability for use in pilot scale GMP manufacturing.
	4-M4		Conduct non GMP stability of BDS and EDP.
	4-D1	Non-Clinical Development	Conduct non-GLP safety studies to include early toxicity in animal models consistent with product's intended use (e.g. route of administration and dose range (small animals may be used)).
	4-D2		Conduct early dose-range PK/PD/biodistribution studies
	4-E1	Non-Clinical Efficacy	Expand on initial proof of concept studies to develop relevant animal model(s). Demonstrate relevance to threat being addressed.
	4-E2		Demonstrate non-GLP in vivo activity and potential for efficacy consistent with the product's intended use (i.e. dose, schedule, duration, route of administration, and route of threat agent challenge)
	4-E3		Initiate assay development to evaluate critical outcomes in both animals and humans.
	4-E4		Evaluate potential biomarkers for measuring efficacy.
	4-C1	Clinical	No Activity.
5		Overview	Advanced Characterization of Candidate and Initiation of GMP Process Development Continue non-GLP in vivo studies, and animal model and assay development. Develop a scalable and reproducible manufacturing process amenable to GMP. Animal Models: Continue development of animal models for efficacy and dose-ranging studies. Assays: Initiate development of in-process assays and analytical methods for product characterization and release, including assessments of potency, purity, identity, strength, sterility, and quality as appropriate. 5A Demonstrate acceptable Absorption, Distribution, Metabolism, and Elimination characteristics and/or immune responses in non-GLP animal studies as necessary for IND filing. 5B Continue establishing correlates of protection, endpoints, and/or surrogate markers for efficacy for use in future GLP studies in animal models. Identify minimally effective dose to facilitate determination of "humanized" dose once clinical data are obtained. *** Changes in formulation require re-evaluation activities to be undertaken at lower TRL levels.
	5-R1	Regulatory	Submit Pre-IND package to FDA and conduct Pre-IND meeting



Q-TRL List

TRL Level	Sub Level	Product Development Area	Q-TRL Description
	5-R2		Prepare draft TPP (Target Product Profile). Questions of shelf life, storage conditions, and packaging should be considered to ensure that anticipated use of the product is consistent with the intended use for which approval will be sought from the FDA.
	5-M1	CMC	Complete development of a pilot scale process for BDS that is amenable to GMP manufacturing
	5-M2		Complete process development for a clinical drug product (CDP) suitable for early clinical studies
	5-M3		Complete development of in-process assays and analytical methods for characterization and release of pilot scale BDS and CDP, including assessments of identity, potency, impurities, sterility, and quality, as appropriate.
	5-M4		Produce BDS and FDP at pilot scale (non GMP) and establish specifications for BDS and CDP.
	5-M5		Initiate stability studies of reagents and reference standards
	5-M6		Perform Tech Transfer to GMP facility (if applicable).
	5-D1	Non-Clinical Development	Measure absorption, distribution, metabolism, and elimination characteristics and/or immune responses in non-GLP animal studies
	5-D2		Complete non-GLP dose-range PK/PD/biodistribution studies
	5-D3		Complete refinement of assays for in vivo PK/PD/biodistribution
	5-E1	Non-Clinical Efficacy	Complete development -of assays that will be used to assess biomarkers.
	5-E2		Optimize drug performance in-vitro.
	5-E3		Optimize drug performance in-vivo.
	5-E4		Demonstrate efficacy (and dose-response) in at least one relevant animal model
	5-C1	Clinical	Develop phase 1 clinical trial protocol synopsis
6		Overview	<p>GMP Pilot Lot Productions, IND Submission, and Phase 1 Clinical Trial(s) Manufacture GMP-compliant pilot lots. Prepare and submit Investigational New Drug package to FDA and conduct Phase 1 Clinical trial. Animal Models: Continue animal model development via toxicology, pharmacology, and immunogenicity studies. Assays: Qualify assays for manufacturing quality control and immunogenicity, if applicable</p> <p>6A Conduct GLP non-clinical studies for toxicology, pharmacology, and immunogenicity as appropriate. 6B Prepare and submit IND package to FDA to support initial clinical trial(s). 6C Complete Phase 1 clinical trial(s) that establish an initial safety, pharmacokinetics and immunogenicity assessment as appropriate.</p>
	6-R1	Regulatory	Prepare and submit Investigational New Drug (IND) to FDA. Include: Elements of the FDA Animal Rule, Conceptual design for efficacy studies
	6-R2		Update Target Product Profile as appropriate.
	6-R3		Conduct end of Phase 1 Meeting with FDA. (only available to Fast Track products)



Q-TRL List

TRL Level	Sub Level	Product Development Area	Q-TRL Description
	6-M1	CMC	Capability to Produce Systems, Subsystems, or Components in a Production Representative Environment Manufacture, release, and conduct stability testing of GMP-compliant bulk (BDS) and formulated product(FDP) in support of the IND and clinical trial(s).
	6-M2		Qualify assays for manufacturing Quality control and potency, as applicable
	6-M3		Qualify candidate reference reagents for these assays
	6-M4		Initiate development of Final Drug Product (FDP) for Phase 2-3 clinical trials.
	6-D1	Non-Clinical Development	Conduct GLP toxicity and PK/PD testing (repeat dose, acute, etc).
	6-E1	Non-Clinical Efficacy	Qualify appropriate critical assays used to assess physicochemical, in vitro and in vivo animal efficacy, PK/PD and/or immunogenic characteristics of the product.
	6-E2		Establish reproducibility of relevant animal model(s) with respect to achieving endpoints.
	6-C1	Clinical	Begin subject enrollment for Phase 1 clinical trial(s) to establish an initial safety, pharmacokinetics and immunogenicity assessment.
	6-C2		Complete last subject last visit for Phase 1 clinical trial(s)
	6-C3		Deliver final clinical study report for Phase 1 clinical trial(s)
7		Overview	Scale-up, Initiation of GMP Process Validation, and Phase 2 Clinical Trial(s) Conduct animal efficacy studies as appropriate. Conduct Phase 2 clinical trial(s). Animal Models: Refine animal model development in preparation for pivotal GLP animal efficacy studies. Assays: Validate assays for manufacturing quality control and immunogenicity, if applicable. 7A Conduct GLP animal efficacy studies as appropriate for the product at this stage. 7B Complete expanded clinical safety trials as appropriate for the product (e.g. Phase 2).
	7-R1	Regulatory	Update Target Product Profile as appropriate.
	7-R2		Conduct End of Phase 2 Meeting with FDA.
	7-R3		Submit amendment(s) for expanded clinical trials.
	7-R4		Approve label for product shipped to SNS.
	7-R5		Submit Special Protocol Assessment for pivotal efficacy studies
	7-M1	CMC	Complete development of final process for licensure/approval, conduct engineering runs and GMP runs at scale compatible with USG requirements
	7-M2		Complete stability studies of the GMP product in a formulation, dosage form, and container consistent with the Target Product Profile in support of label expiry dating.
	7-M3		Perform appropriate shipping validation
	7-M4		Obtain QA approval of process validation plan
7-M5		Validate assays used to assess product quality and complete assay validation package	



Q-TRL List

TRL Level	Sub Level	Product Development Area	Q-TRL Description
	7-D1	Non-Clinical Development	Conduct reproductive toxicology studies (small animals may be used).
	7-E1	Non-Clinical Efficacy	Validate assays used to assess critical outcomes in clinical trials and in animal efficacy studies.
	7-E2		Complete refinement of animal model development in preparation for pivotal GLP animal efficacy studies
	7-E3		Transfer animal models to GLP facility, if necessary, and conduct studies sufficient to demonstrate successful transfer.
	7-C1	Clinical	Begin subject enrollment for expanded human clinical trials - Phase 2 studies (as needed).
	7-C2		Complete last subject last visit for Phase 2 clinical trial(s)
	7-C3		Deliver final clinical study report for Phase 2 clinical trial(s)
	7-C4		Evaluate human biologic outcomes in Phase 2 clinical studies using validated assays and properly qualified reference QC reagents
		Overview	<p>Completion of GMP Validation and Consistency Lot Manufacturing, Pivotal Animal Efficacy Studies or Clinical Trials, and FDA Concurrence or Licensure Finalize GMP manufacturing process. Complete pivotal animal efficacy studies or clinical trials (e.g. Phase 3), and/or expanded clinical safety trials as appropriate. Prepare and submit NDA/BLA.</p> <p>8A Complete pivotal GLP animal efficacy studies or pivotal clinical trials (e.g. Phase 3), and any additional expanded clinical safety trials as appropriate for the product.</p> <p>8B Prepare and submit New Drug Application (NDA) or Biologics License Application (BLA) to the FDA.</p> <p>8C Obtain FDA Approval or licensure.</p>
8	8-R1	Regulatory	Finalize Target Product Profile in preparation for FDA Approval/Licensure.
	8-R2		Obtain FDA concurrence on animal model(s) for pivotal animal efficacy studies and Phase 3 studies
	8-R3		Conduct Pre- New Drug Application (NDA) or Biologics Licensing Application (BLA) meeting with the FDA.
	8-R4		Prepare and submit New Drug Application (NDA) or Biologics License Application (BLA) to the FDA.
	8-R5		Obtain FDA approval or licensure.
	8-M1	CMC	Complete GMP validation for manufacturing quality control, potency, and produce consistency lots or registration lots at a scale compatible with USG requirements and/or required for licensure.
	8-M2		Continue long term stability studies to extend expiry dating.
	8-M3		Produce initial product stockpile quantities
	8-M4		Complete appropriate shipping validation
	8-D1	Non-Clinical Development	No Activity.
	8-E1	Non-Clinical Efficacy	Conduct pivotal animal GLP efficacy studies using final product formulation and use appropriate statistical to meet the requirements of the BLA/NDA submission.
	8-C1	Clinical	Begin subject enrollment for Phase 3 clinical trial
	8-C2		Complete last subject last visit for Phase 3 clinical trial



Q-TRL List

TRL Level	Sub Level	Product Development Area	Q-TRL Description
	8-C3		Deliver final clinical study report for Phase 3 clinical trial
	8-C4		Evaluate critical biologic outcomes In Phase III clinical trials using validated assays and properly qualified reference and QC reagents.
		Overview	Post-Licensure and Post-Approval Activities 9A Commence post-licensure/post-approval and Phase 4 studies (post-marketing commitments) 9B Maintain manufacturing capability as appropriate.
	9-R1	Regulatory	Commence post-licensure/post-approval and Phase 4 studies (post marketing commitments) such as safety surveillance, studies to support use in special populations, and clinical trials to confirm safety and efficacy as feasible and appropriate.
	9-R2		Re-label investigational product in SNS with approved/licensed labeling
	9-M1	CMC	Complete delivery of contracted amount of approved or licensed product to stockpile
9	9-M2		Transfer and cross-validate assays in additional facilities, if necessary.
	9-M3		If using challenge potency assays, identify alternatives, compare and validate new assay.
	9-M4		Maintain manufacturing capability as appropriate.
	9-D1	Non-Clinical Development	No Activity.
	9-E1	Non-Clinical Efficacy	Transfer animal model to additional facilities, if necessary.
	9-C1	Clinical	Begin subject enrollment for Phase 4 studies
	9-C2		Complete last subject last visit for Phase 4 studies
	9-C3		Deliver final clinical study report for Phase 4 studies



Harmonized Q-TRL List for Diagnostics MCMs

The US Department of Health and Human Services (HHS) and the Department of Defense (DoD) are engaged in the development of medical countermeasures (MCM) for Chemical, Biological, Radiological and Nuclear (CBRN) threats. The DoD and HHS utilize harmonized Technology Readiness Levels (TRLs) as a common method to understand at a general level the maturity of MCM development products in development across the USG. TRLs consist of nine progressive levels of milestones over a product development lifecycle.

Quantitative Technological Readiness Levels (Q-TRLs) expand the nine high-level TRLs to a much more detailed level to provide key development milestones and activities specific to vaccine, small molecule, biologics and diagnostics. These Q-TRLs are not intended to be a requirement for each project but rather to provide a selection of milestones and activities throughout the development lifecycle from discovery through post-approval.

Naming Conventions

For the Diagnostics Q-TRL naming conventions the first number denotes TRL level, D denotes diagnostics, the second letter denotes functional areas, last number is sequential number of Q-TRL in a functional area. DPM is Program Management, DR is Regulatory, DREQ is Requirements, DRES is Research & Dev, DAS is Animal Studies, DCS is Clinical Studies, DAD is Assay Dev, DID is Instrument Dev, DQ is Quality, DAM is Assay Mfg and DIM is Instrument Mfg.



Q-TRL List for Diagnostics

TRL Level	Sub Level	Product Development Area	Q-TRL Description
1		Overview	Review of Scientific Knowledge - Active monitoring of scientific knowledge base to identify clinical pathological markers for diagnostic countermeasure candidates. Scientific findings are reviewed and assessed as a foundation for characterizing approaches to intervene in disease. Basic research needs identified.
	1-DPM1	Program Management	No activity.
	1-DR1	Regulatory	No activity.
	1-DREQ1	Requirements	Assess clinical and/or public health needs.
	1-DRES1	Research & Dev	Review the clinical pathology of human disease (or specific medical conditions) attributed to specific threat agents and documented experience with diagnostic testing for both clinical management and for public health, national security objectives (e.g., early recognition).
	1-DRES2	Research & Dev	Review natural/case history studies and available data/information.
	1-DAS1	Animal Studies	No activity.
	1-DCS1	Clinical Studies	No activity.
	1-DAD1	Assay Dev	No activity.
	1-DID1	Instrument Dev	No activity.
	1-DQ1	Quality	No activity.
	1-DAM1	Assay Mfg	No activity.
	1-DIM1	Instrument Mfg	No activity.
1-DIV1	Integration & Verification	No activity.	
2		Overview	Concept Generation and Development of Experimental Designs - Develop research plans to answer specific questions and experimental designs for addressing the related scientific issues and to establish feasibility. Focus on practical applications based on basic principles.
	2-DPM1	Program Management	Conduct feasibility phase readiness review and prepare approval report.
	2-DR1	Regulatory	No activity.
	2-DREQ1	Requirements	Prepare preliminary design inputs, test and instrument performance specifications and user needs assessment (ISO 9001 and 1345).
	2-DRES1	Research & Dev	Conduct and evaluate a market survey (currently existing solutions) and a literature search (state of the art).
	2-DRES2	Research & Dev	Characterize threat agent and clinical parameters to verify disease etiology; identify candidate diagnostic targets.
	2-DRES3	Research & Dev	Develop a product concept.
	2-DRES4	Research & Dev	Document feasibility regarding use of existing technological platform/methodology to meet preliminary requirements.
	2-DAS1	Animal Studies	Perform non-GLP small animal studies to support research (if needed).
	2-DAS2	Animal Studies	Demonstrate relevance of animal models to defined human disease threat(s).
2-DCS1	Clinical Studies	No activity.	



	2-DAD1	Assay Dev	Develop/Identify candidate assay technologies to support test system concept.
	2-DID1	Instrument Dev	Develop/Identify candidate instrument / automation technologies to support test concept. [high risk without first establishing assay feasibility].
	2-DQ1	Quality	No activity.
	2-DAM1	Assay Mfg	No activity.
	2-DIM1	Instrument Mfg	No activity.
	2-DIV1	Integration & Verification	No activity.
		Overview	Characterization of Preliminary Candidates(s) and Feasibility Demonstration - Begin R&D, data collection, and analysis in order to verify feasibility. Explore alternative concepts, identify and evaluate critical technologies and components, and begin characterizing specifications required. Demonstrate the performance of candidate diagnostic targets and high risk components. Develop a business case for the proposed product.
	3-DPM1	Program Management	Conduct product feasibility review and prepare approval report [would be requirement/gate to move to TRL4].
	3-DPM2	Program Management	Prepare estimate of each system critical component, non-critical component cost & price and development cost along with projected timelines.
	3-DPM3	Program Management	Identify key development team organizations, both internal and external. Initiate commercial discussions with external team members.
	3-DPM4	Program Management	Prepare Intellectual Property report detailing initial patentability, freedom to operate, and licenses needed.
	3-DR1	Regulatory	Prepare initial regulatory strategy document including intended use statement, analytical and clinical study plans, and specimen requirements.
	3-DREQ1	Requirements	Define preliminary high level test system requirements & critical component and assay specifications.
3	3-DRES1	Research & Dev	Research and characterize diagnostic targets and identify chemistries, reagents needed to detect or quantify.
	3-DRES1	Research & Dev	Prepare body of data to demonstrate feasibility of final test system concept with preliminary experiments to detect, quantify selected diagnostic targets.
	3-DRES1	Research & Dev	Determine preliminary development risks.
	3-DAS1	Animal Studies	Perform GLP studies to validate a potential diagnostic target's usefulness.
	3-DCS1	Clinical Studies	Conduct experiments with archived clinical samples [pre-clinical studies (if applicable)] to demonstrate diagnostic targets assay feasibility.
	3-DAD1	Assay Dev	Develop high level assay design based on requirements.
	3-DAD2	Assay Dev	Demonstrate feasibility of high technical risk assay components and technologies for laboratory experiments.
	3-DID1	Instrument Dev	Develop high level device/instrument architecture; assess engineering, SW risks if OTS components not available, require customization, redesign.
	3-DID2	Instrument Dev	Demonstrate feasibility of high technical risk device/instrument components and technologies with prototypes demonstrating feasibility of throughput and limit of detection, or obtain OTS critical components. Produce non-GMP prototypes.
	3-DQ1	Quality	Identify reagents, materials and test methods that will be used for assessing specifications.



	3-DAM1	Assay Mfg	No activity.
	3-DIM1	Instrument Mfg	No activity.
	3-DIV1	Integration & Verification	No activity.
		Overview	Optimization and Preparation for Assay, Component, and Instrument Development – Prepare for test system development. Finalize diagnostic target(s) and methods for detecting or quantitating target(s). Develop detailed plans and finalize critical design requirements. Execute commercial agreements with key external development partners. Identify manufacturing resources, vendor sourcing, and experimental designs.
4	4-DPM1	Program Management	Develop a detailed project plan.
	4-DPM2	Program Management	Negotiate commercial agreements with external team members for product development activities.
	4-DPM3	Program Management	Finalize system architecture and freeze requirements for initial development.
	4-DPM4	Program Management	Conduct system development readiness review and prepare approval report.
	4-DR1	Regulatory	Prepare a detailed regulatory strategy document, including draft intended use statement, analytical and clinical study plans and specimen requirements.
	4-DQ1	Quality	Develop and begin implementation of a Quality Management System.
	4-DREQ1	Requirements	Begin detailed requirements definition, hardware, software, assays.
	4-DREQ2	Requirements	Initiate user's interface definition.
	4-DRES1	Research & Dev	Finalize diagnostic targets assays (mechanism for detecting selected diagnostic targets through focused experiments).
	4-DRES2	Research & Dev	Complete tech transfer from Research to Development.
	4-DAS1	Animal Studies	Continued animal studies, as required, to support assay development and assay design finalization.
	4-DCS1	Clinical Studies	Continued pre-clinical studies, as required, to support assay development and diagnostic targets finalization.
	4-DAD1	Assay Dev	Finalize Assay requirements and specification.
	4-DID1	Instrument Dev	Finalize initial instrument / device / software architecture.
	4-DID2	Instrument Dev	Define design inputs/ outputs and architectures for modules / subsystem.
	4-DAM1	Assay Mfg	Support assay architecture development, providing input on manufacturability of proposed product.



	4-DIM1	Instrument Dev	Support instrument / device architecture development, providing input on manufacturability of proposed product. [if concurrent engineering, need to have bridging studies to assay or reiterative approach with experiments and verification studies using the test system in final design form].
	4-DIV1	Integration & Verification	No activity.
5		Overview	Product Development – Reagents, components, subsystems and modules - Develop reagents and buffers. Build and test non-GLP prototypes of components and subsystems. Code and unit test software. Begin pilot scale manufacturing preparations. Develop protocols for assay and integration testing. Initiate reagent stability testing. Hold pre-IDE meeting with FDA.
	5-DPM1	Program Management	Conduct integration readiness review and prepare approval report.
	5-DR1	Regulatory	Hold pre-IDE meeting with FDA (May occur at earlier TRL, FDA encourages pre-IDE meeting as early as possible)
	5-DR2	Regulatory	Finalize risk management plan and determine effectiveness of mitigations.
	5-DREQ1	Requirements	Finalize user's interface specification.
	5-DREQ2	Requirements	Update requirements and interface control documents as design progresses. Update specifications as components are tested.
	5-DRES1	Research & Dev	No activity.
	5-DAS1	Animal Studies	Provide samples as needed to support assay development (pre-clinical).
	5-DCS1	Clinical Studies	Provide samples as needed to support assay development (pre-clinical).
	5-DAD1	Assay Dev	Produce initial assay lots with quantities sufficient to initiate stability studies.
	5-DAD2	Assay Dev	Demonstrate sensitivity and specificity of prototype assay when performed manually or with standard laboratory methodologies.
	5-DAD3	Assay Dev	Initiate real-time stability studies of reagents with available development lots.
	5-DID1	Instrument Dev	Build and test components and subsystems.
	5-DID2	Instrument Dev	Make preparations for and build Alpha instruments in a non-GMP environment.
	5-DID3	Instrument Dev	Code and unit test software modules.
	5-DID4	Instrument Dev	Produce user's interface simulator and evaluate user's interface. Finalize user's interface definition [may be incorporated at later stage with less risk].
	5-DID5	Instrument Dev	Build 1 st release of instrument software for integration testing.
	5-DQ1	Quality	Freeze design documents for alpha instrument/device build and laboratory assay production.
	5-DQ2	Quality	Initiate Design History File and Device Master Record [this would be done only when all priority requirements are met for both instrument and assay, reagents].
	5-DAM1	Assay Mfg	Make preparations (documents, process, procedures, etc.) for scaled development lots in a GMP compliant process with concurrent document development. Initiate design controls. [gateway to TRL6].



	5-DIM1	Instrument Mfg	Identify/build pilot instrument/device manufacturing facility, Make preparations (documents, process, procedures, etc.) for pilot Mfg build of beta instruments and components at pilot scale in a GMP compliant process. Order tooling and equipment necessary.
	5-DIV1	Integration & Verification	Prepare protocols and test procedures for assay / system integration and testing. Prepare for alpha instrument testing.
6		Overview	System integration & testing - Integrate and test alpha and beta instruments/devices, software and assays, evaluating performance and updating specifications. Implement design improvements to address defects discovered during testing. Produce and evaluate pilot lots of reagents and beta (pilot) instruments. Increase the maturity of software. Prepare for clinical testing. Complete short term stability testing of reagents.
	6-DPM1	Program Management	Conduct analytical verification readiness review and prepare approved report.
	6-DR1	Regulatory	Hold pre-IDE discussion with FDA/CDRH to finalize regulatory strategy and pathway, e.g., clearance (510k), approval (PMA), pre-authorization (pre-EUA), or CLIA Waiver.
	6-DR2	Regulatory	Submit preliminary filings to the FDA to determine class of diagnostic (e.g., Class I, II, III) and what route of submission (e.g., clearance (510k), approval (PMA), etc.) is required.
	6-DREQ1	Requirements	Update product specifications to ensure requirements are met.
	6-DRES1	Research & Dev	No activity.
	6-DAS1	Animal Studies	If applicable, prepare protocols, apply/receive IACUC approvals for further studies.
	6-DCS1	Clinical Studies	Prepare clinical study protocols; identify test sites, IRB approval and informed consent as required.
	6-DAD1	Assay Dev	Support integration testing. Evaluate / resolve design defects discovered.
	6-DAD2	Assay Dev	Finalize test QC materials and protocols.
	6-DAD3	Assay Dev	Complete assay testing & characterization studies. Complete short term testing of reagents.
	6-DID1	Instrument Dev	Support integration testing. Evaluate / resolve design defects discovered.
	6-DQ1	Quality	Evaluate documentation and pilot manufacturing processes to ensure GMP compliance.
	6-DAM1	Assay Mfg	Produce pre-clinical lots of reagents in per process under document control.
	6-DIM1	Instrument Mfg	Produce beta instrument per process under document control.
	6-DIV1	Integration & Verification	Complete hardware/software/assay integration and verification testing.
	6-DIV2	Integration & Verification	Prepare protocols for analytical and pre-clinical testing.
			Overview
7	7-DPM1	Program Management	Perform review and approval of design verification report.
	7-DPM2	Program Management	Conduct clinical readiness review and prepare approval report.



	7-DR1	Regulatory	Develop and approve labeling including IFU for investigational test system.
	7-DR2	Regulatory	Obtain FDA feedback on clinical validation (use of animal samples as applicable, animal rule does not apply to Dx)).
	7-DREQ1	Requirements	Track verification activities per product validation matrix.
	7-DRES1	Research & Dev	No Activity.
	7-DAS1	Animal Studies	Provide animal samples as required to support analytical verification testing.
	7-DCS1	Clinical Studies	Provide human samples as required to support analytical verification testing.
	7-DCS1	Clinical Studies	Complete identification, sourcing and distribution of clinical test lots. Distribute clinical test protocols and site binders, monitor progress.
	7-DAD1	Assay Dev	Support analytical verification testing. Evaluate / resolve/document design defects discovered.
	7-DID1	Instrument Dev	Support analytical verification testing. Evaluate / resolve design defects discovered.
	7-DQ1	Quality	Monitor analytical testing results. Ensure design controls Under Quality Systems Regulations.
	7-DAM1	Assay Mfg	Produce additional clinical lots with real-time stability.
	7-DAM2	Assay Mfg	Perform appropriate shipping validation.
	7-DIM1	Instrument Mfg	Produce additional beta instruments for clinical evaluations, if required.
	7-DIM2	Instrument Mfg	Perform appropriate shipping validation.
	7-DIV1	Integration & Verification	Verify that the diagnostics system meets it specifications and requirements through testing of contrived, retrospective human, normal human and animal samples through execution of a design verification protocol (containing defined study endpoints).
		Overview	Clinical Studies and/or evaluation with Animal Studies, FDA Clearance or Approval, Finalize GMP manufacturing preparations - Complete clinical evaluations. Prepare and submit FDA filing. End of TRL8: Acquire FDA approval, or clearance.
8	8-DPM1	Program Management	Conduct FDA filing readiness review and prepare approval report.
	8-DR1	Regulatory	Compile clinical validation and animal study data (where applicable).
	8-DR2	Regulatory	Prepare regulatory filing.
	8-DR3	Regulatory	Submit filing to FDA when ready and approved.
	8-DR4	Regulatory	Coordinate activities with FDA. Coordinate response to FDA questions/ notifications. Obtain Approval, Clearance, or pre-authorization, or CLIA Waiver.
	8-DREQ1	Requirements	Finalize product specifications.
	8-DRES1	Research & Dev	No Activity.
	8-DAS1	Animal Studies	Perform pivotal GLP animal studies per approved protocols to validate system performance.
	8-DAS2	Animal Studies	Complete final animal study CSR.
	8-DCS1	Clinical Studies	Perform clinical evaluation per approved protocols to validate diagnostic system performance. Manage clinical sites.



	8-DCS2	Clinical Studies	Complete final human clinical study CSR.
	8-DAD1	Assay Dev	Support pivotal animal studies and clinical evaluations. Evaluate / resolve design defects discovered.
	8-DID1	Instrument Dev	Support pivotal animal studies and clinical evaluations. Evaluate / resolve design defects discovered.
	8-DQ1	Quality	Monitor clinical and animal study processes and documentation to ensure Regulatory compliance.
	8-DAM1	Assay Mfg	No activity.
	8-DIM1	Instrument Mfg	Develop maintenance, other tech support.
	8-DIV1	Integration & Verification	Support pivotal animal studies and clinical evaluations. Evaluate / resolve design defects discovered. Instruct clinical sites on use of the diagnostic system.
		Overview	Post-Clearance / Post-Approval Activities Perform post market surveillance, field studies in designated sites; monitor performance, reliability, fitness for use. Establish and maintain appropriate Quality Systems compliant manufacturing capability/inventory Deliver USG ordered product if applicable.
9	9-DPM1	Program Management	No activity.
	9-DR1	Regulatory	Establish acquisition mechanism for monitoring, Post Marketing Data Performance (if required), complaint handling.
	9-DR2	Regulatory	Perform post marketing surveillance as required.
	9-DREQ1	Requirements	No activity.
	9-DRES1	Research & Dev	No activity.
	9-DAS1	Animal Studies	No activity.
	9-DCS1	Clinical Studies	No activity.
	9-DAD1	Assay Dev	Continue long term stability studies to extend expiry dating.
	9-DID1	Instrument Dev	No activity.
	9-DQ1	Quality	Fully implemented Quality Management System.
	9-DQ2	Quality	QMS monitoring of manufacturing processes to ensure GMP compliance.
	9-DAM1	Assay Mfg	Identify/build full scale GMP compliant assay manufacturing capacity, if pilot capacity insufficient. Validate processes and performance.
	9-DAM2	Assay Mfg	Produce initial assay stockpile quantities.
	9-DAM3	Assay Mfg	Maintain manufacturing capability as appropriate.
	9-DAM4	Assay Mfg	Provide field support.
	9-DIM1	Instrument Mfg	Identify/build full scale GMP compliant instrument/device manufacturing capacity, if pilot capacity insufficient, Validate all processes and performance.
	9-DIM2	Instrument Mfg	Produce initial instrument/device stockpile quantities.
9-DIM3	Instrument Mfg	Maintain manufacturing capability as appropriate.	
9-DIM4	Instrument Mfg	Provide sustaining engineering field support.	



FINAL – For PUBLIC USE

	9-DIV1	Integration & Verification	No Activities.
--	--------	----------------------------	----------------