AMENDMENT 1

AMENDMENT OF BARDA BROAD AGENCY ANNOUNCEMENT
Therapies for Hematopoietic Syndrome, Bone Marrow Stromal Cell Loss, and Vascular Injury Resulting From Acute Exposure to Ionizing Radiation

Solicitation Number:	BAA-BARDA-08-08
Amendment Number:	One (1)
Amendment Issue Date:	Thursday, March 27, 2008
Proposal Due Date: (UNCHANGED)	**Thursday, April 17, 2008 at 4:00 P.M. DST Local Time**
Issued By:	Contracting Officer Biomedical Advanced Research and Development Authority 330 Independence Avenue, S.W. Room G644 Washington, D.C. 20201
Point of Contact:	Carl A. Newman, Contract Specialist E-mail: carl.newman@hhs.gov

This amendment is issued to all Interested Parties and Offerors.

This amendment is issued for clarification purposes and does NOT MATERIALLY CHANGE THIS REQUIREMENT. Except as provided herein, all terms and conditions of the Broad Agency announcement (BAA) remain unchanged and in full force and effect.

The purpose of this amendment is to:

1. **change the room number in the Independence Avenue, S.W. address from G640 to G644,**
2. **add an address for hand delivery of the proposals,**
3. **clarify the page limitation for the Statement of Work shall be 15 pages,**
4. **increase the percentage goal for subcontracting with small business concerns,**
5. **add the Security Requirement attachment,**
6. **note the maximum dimensions of the proposal box size,**
7. **clarify the time of review for clinical trial protocols,**
8. **answer a number of inquiries.**

1. Change all references to the Independence Avenue, S.W. address

From: 330 Independence Ave, S.W.
Room G640
Washington, D.C. 20201

To: 330 Independence Ave, S.W.
Room G644
Washington, D.C. 20201

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2. Under page 1, Block 18 (Hand Delivery or Overnight Service) is deleted and replaced as follows:

Overnight service includes courier services such as FedEx, UPS, and DHL. Use the address in Block 19, as changed by paragraph 1 above. Hand delivery is discouraged due to the difficulty in unloading vehicles near the building entrance. However, if the proposals will be hand-delivered, please contact the Contract Specialist 24 hours prior to the delivery of proposals. The address for hand delivery follows:

Carl A. Newman, Contract Specialist
Biomedical Advanced Research and Development Authority (BARDA)
Mary E. Switzer Memorial Building East
300 C. Street, S.W.
Room 3124
Washington, DC 20201

3. Under page 3, **DESCRIPTION**, the second paragraph shall now read as follows:

A proposal submitted in response to this BAA must present a detailed technical and cost proposal designed to meet the Research and Technical Objectives described in this announcement. The proposal must be signed by an official authorized to contractually commit the submitting organization. The Statement of Work (SOW), including the specific work requirements and performance specifications, is developed and defined by the Offeror, not the USG. The SOW should not exceed fifteen (15) single spaced-pages (in 12 pt font, Times New Roman) in length within the technical proposal, which is limited to two hundred (200) pages total (including all appendices and attachments).

4. Under page 48, **INSTRUCTIONS, CONDITIONS, AND NOTICES TO OFFERORS**, **BUSINESS PROPOSAL INSTRUCTIONS**, paragraph d (Small Business Subcontracting Plan), subparagraph d, item 11 is deleted and replaced as follows:

List the types of records the offeror will maintain to demonstrate procedures that have been adopted to comply with the requirement and goals in the plan, including establishing source lists. Also, the offeror shall describe its efforts to locate Small, Small Disadvantaged, Women-Owned, HUBZone, Veteran-Owned, and Service Disabled Veteran-Owned Small Businesses and award subcontracts to them.

For additional information about each of the above elements required to be contained in the subcontracting plan, see FAR Clause 52.219-9, Small Business Subcontracting Plan, and the Sample Subcontracting Plan which is provided as an attachment to this BAA.

HHS expects each procuring activity to establish minimum subcontracting goals for all procurements. The anticipated minimum goals for this BAA are as follows:

39.9 % for Small Business; 5 % for Small Disadvantaged Business; 5 % for Women-Owned Small Business; 3 % for HUBZone Small Business; and 3 % for Veteran-Owned Small Business and 3% for Service-Disabled Veteran-Owned Small Business.

5. Under page 57, **LIST OF ATTACHMENTS**, Attachment A (Security Requirement) is added.

6. Under page 58, **LIST OF ATTACHMENTS**, Attachment B (**PACKAGING AND DELIVERY OF THE PROPOSAL)** is revised and added.

7. Under page 96, **Attachment 16, V. Deliveries or Performances, Technical Reports, Clinical Trial Protocols** is deleted and replaced as follows:

Clinical Trial Protocols	1 Original 1CD 1 Copy 1 CD	*Contracting Officer* BARDA 330 Independence Ave, S.W. Room G644 Washington, D.C. 20201 *Project Officer* BARDA 330 Independence Ave. S.W. Room G644 Washington, D.C. 20201	To be negotiated with the BARDA Contracting Officer prior to IND submission or enrollment of human subjects, whichever is earlier. BARDA will complete the review of the Clinical Trial Protocols 30 days from receipt.

8. The following are questions submitted by offerors and responses provided by BARDA.

Question 1: Can BARDA or NIAID provide a list of qualified animal investigators for GLP and non-GLP animal radiation studies?
Answer 1: Please network through academic and industry contacts.

Question 2: Are there regional centers supported by NIAID that specialize in these types of animal models?
Answer 2: Refer to the NIAID web address http://www3.niaid.nih.gov/ .

Question 3: Who would be the most appropriate person in the government to discuss this with?
Answer 3: **The point of contact for this Broad Agency Announcement is Carl Newman whose phone number and e-mail respectively are 202-205-1156 and carl.newman@hhs.gov.**

Question 4: What sorts of products would be responsive to Research Area 3?
Answer 4: If the product improves vascular integrity, then it is responsive to the BAA Research Area 3.

Question 5: Will this BAA support development of additional cytokines for treating neutropenia?
Answer 5: BARDA will consider broad spectrum cytokine therapies that ameliorate the hematopoietic syndrome (neutropenia, thrombocytopenia, lymphopenia and anemia).

Question 6: Does Research Area 2 encompass cytokines and growth factors that enhance bone marrow transplantation into radiated humans or is bone marrow transplantation not being considered as a possible treatment?
Answer 6: Research area 2 covers the development of medical countermeasures to replenish bone marrow niche and progenitor cells that normally populate the marrow stroma and niche environment and that can, following acute exposure to ionizing radiation that induces lethal hematopoietic dyscrasias, restore normal functioning hematopoietic cell lineages.

Question 7: The solicitation indicates that funds can be used for Phase 2 clinical studies. Does this mean Phase 2 clinical studies in another clinical indication towards FDA approval of the drug such as chemotherapy-induced neutropenia in cancer patients or is the Phase 2 clinical trial limited to radiation exposure (which can't be done with humans)?
Answer 7: The purpose of the BAA is advanced development for products that will be efficacious in treating radiation injury. It is within the scope of the BAA to support Phase 2 safety studies along with efficacy studies under the FDA "animal rule" when human studies are not appropriate.

Question 8: Can NIH or other government agencies provide GMP protein manufacturing services, formulation and stability testing services, toxicology services, etc. for small companies to assist in development of candidates responsive to this solicitation? If so, who would be the best contact person?
Answer 8: BARDA does not provide these services. Please contact other government agencies regarding their capabilities.

Question 9: It isn't clear whether cost or score is more important in selecting successful proposals. Could you elaborate on the relative value of these?
Answer 9: An Order of Merit is established which includes the offeror's score and whether they are rated technically acceptable or technically unacceptable. Technically acceptable offerors are eligible for selection, negotiations and a potential award based on the evaluation criteria on pages 18-21. In addition evaluation factors including cost, technical and others are prioritized under Evaluation Factors for Award, paragraph 1 (General), page 18. "Although technical factors are of paramount consideration in the award of the contract, BARDA program priorities, cost/price, past performance, and SDB participation are also important to the overall contract award decision."

Question 10: Would the combination new chemical entity (NCE) plus an approved drug be considered a "single agent" (page 6 scope (b)) under this program?
Answer 10: Any regulatory decision regarding a Medical Countermeasure (MCM) being a single agent will be determined by the Food and Drug Administration (FDA). For purposes of this solicitation, a combination drug containing more than one active ingredient is responsive.

Question 11: On page 3 of the BAA announcement, it states that the SOW should be no longer than 10 pages. However, on page 60 it states the SOW should be no longer than 15 pages. Please Clarify.
Answer 11: Refer to Item 3 of this amendment.

Question 12: Can you give us an estimate for the time required for BARDA to review clinical trial protocols?
Question 12: See Item 7 of this Amendment.

Question 13: Page limitation(s). Through the document, BARDA consistently states the technical proposal should be no longer than 200 pages. However, on page 58, this page limitation appears to also include the business proposal. Is this the case? If not, what is the page limitation for the business proposal?
Answer 13: The technical proposal has a limitation of 200 pages. There are no page limitations for the business proposal.

Question 14: The research and development areas are listed on page 4. Then on page 60, the instructions suggest that if a company's drug candidate fits into more than one of these research and development areas, separate, duplicate proposals are required to be considered for more than one research and development area. Is this correct? If so, should the research and development area be stated on the first page?
Answer 14: If a company's drug candidate fits more than one of the research and development areas, a separate proposal shall be submitted for each research and development area for which you are applying. Refer to Note 1 on page 60. The research and development areas should be stated on the first page of the proposal.

Question 15: If an offeror is scored high enough for an award in two different research and development areas, with duplicate proposals, how many awards will be made?
Answer 15: Refer to the description of the Broad Agency Announcement on page 3 and Evaluation Factors for Award, paragraph 1 (General) on page 18.

Question 16: Would HHS/BARDA accept a CWBS/Gantt chart structure? If so, can it be submitted in a large paper format (approximately 3 feet x 3 feet)?
Answer 16: Yes. BARDA is expecting electronic submission from which BARDA can print 3 x 3 foot WBS/Gantt charts in Project, WORD, EXCEL and PDF.

Question 17: Note Section 9.7 on page 64. In reference to the letter of understanding (LOU), does this refer only to collaborators or does it also included subcontractors?
Answer 17: This should include all collaborators including subcontractors.

Question 18: Could you please clarify the differences between PI and Program Manager?
Answer 18: Principal Investigator- Qualified person designated by the offeror's institution to direct a research project or program who oversees scientific and technical aspects of the day-to-day management of the research.
Program Manager supervises and directs the work of Project Officers and/or Project Managers of the offeror's institution engaged in managing and monitoring the performance under contracts.

Question 19: Must the therapeutic agent proposed be an agent for which an IND has been filed with FDA for any indication more than 30 days before the Offeror submits its Final Proposal Revision.
Answer 19: No. However, the status of the IND will be taken into consideration as one of the evaluation criteria.

Question 20: There are several papers that support different definitions of 'acute exposure'. Do you have any guidance on a specific range or can you confirm that the data we have collected for this range fits the solicitation?
Answer 20: In the case of a radiological/nuclear event, individuals could be exposed to radiation at ≥2 Gy. This level of radiation exposure could result in what is clinically defined as Acute Radiation Syndrome (ARS). Further information can be found in HHS-BARDA-08-10 (Advanced Therapeutics for Treating Neutropenia Resulting from Acute Exposure to Ionizing Radiation)
http://www.fbo.gov/spg/HHS/OOS/OASPHEP/HHS%2DBARDA%2D08%2D10/Attachments.html

Question 21: How will the efficacy of the therapeutic for ARS at 24 hours be evaluated given the use of the animal models under the animal rule and given the difference in metabolic rates for different species. Specifically, my question relates to mice data at 24 hours post radiation. This time point is estimated to actually be equivalent to over one week in a human given the differences in metabolic rates.
Answer 21: In the technical proposal, BARDA will evaluate the adequacy and validity of the animal model. It is the responsibility of the Offeror to provide sufficient information. A product that is used 24 hours post exposure is responsive to the solicitation.

Question 22: Are transplant approaches responsive to BAA 08-08?
Answer 22: Yes.

Question 23: The BARDA instructions state that only a single agent can be investigated. Is it appropriate to propose combinations of therapeutic agents?
Answer 23: Only a single product may be investigated per proposal. However, a single drug product (agent) may have more than one active ingredient. Therefore, a combination product is acceptable if submitted as a single agent.

Question 24: The treatments we are investigating have been licensed for clinical use. Is it sufficient to propose studies in whole animals, i.e., mice, or would primate studies need to be proposed?
Answer 24: It is incumbent upon each Offeror to submit a research plan that is appropriate for their proposed product.

Question 25: Is it appropriate to propose clinical trials in normal human volunteers or data from two animal species which would reasonably allow translation to normal humans through application of the "animal rule"?
Answer 25: The regulatory pathway will be determined by the FDA at the appropriate time.

Question 26: We have several possible treatments for a particular area within the BAA. Which one should we submit?
Answer 26: It is preferred that the proposed agent be at a development level of an IND or greater. Whether you propose one or both agents is your decision. What you submit is your professional judgment. However it is limited to one agent for each designated research area.

END OF AMENDMENT #1 to BAA BARDA-08-08