Supplement to the United States Army Medical Research and Materiel Command Broad Agency Announcement 06-1: Lyophilized Human Plasma for Combat Casualty Care Call for Pre-Proposals

FOR THIS SUPPLEMENT ONLY, PREPROPOSALS MAY NOT BE SUBMITTED ELECTRONICALLY THROUGH THE USAMRAA WEBSITE. HARDCOPY OR ELECTRONIC FORMAT PREPROPOSALS WITH THE THREE REQUIRED PRODUCT SAMPLES WILL ONLY BE ACCEPTED AT THE USAMRAA ADDRESS LISTED UNDER SUBMISSION BELOW.

SUBJECT: This acquisition effort is being initiated to support the advanced development research efforts required for United States (U.S.) Food and Drug Administration (FDA) approval of a lyophilized human plasma.

DESCRIPTION: Fresh Frozen Plasma (FFP) imposes a significant logistical burden on the U.S. Armed Forces during combat operations. In order to reduce that burden and provide plasma to additional units within the Combat Hospital System, the U.S. Army Medical Research and Materiel Command is seeking to fund advanced development research supporting FDA approval of a lyophilized human plasma.

PROPOSAL: Pre-proposals will include three sections: cover sheet, technical description, and data. All sections will be completed using Times New Roman, 12 point black font with 1" margins. Non-conforming proposals will not be evaluated. The cover sheet will include: Title, organization name and principal contacts, any partnering arrangements and contacts, duration of the project, estimated cost to the Army for each year, and key participating personnel. The technical description will address the technical requirements listed below. It will be double spaced and have a maximum length of 8 pages. Data supporting the technical description will be displayed in table or graph format in the data section. There is no limit to the number of data pages, but common sense should apply. Three product samples from three separate lyophilization runs, in current product packaging, and the MRMC materiel transfer agreement must be submitted along with the pre-proposal. These samples may be tested or otherwise consumed during the evaluation process. Aliquots of any reconstituted samples will be retained in the WRAIR repository during the evaluation, and then destroyed as biohazardous waste.

PROPOSAL TECHNICAL REQUIREMENTS:
Please provide the following information and data to the extent they are available.

a. Maturity of product:
   i. Description of current product
      1. Raw materiel source
      2. Processing
      3. Intermediate product specification
      4. Packaging
         a. Volume
         b. Material
         c. Reconstitution method

5. Stability Data
    a. Intermediate product
    b. Final product

ii. General stage of research development efforts: pre-clinical, clinical, licensing application filed, approved (list countries)

iii. In vitro test assays and results (required);
    1. Characterization - At a minimum, the pre-proposal should include lab normal values, and pre- and post-lyophilization values (from the same donor or pool) for the following characteristics:
        a. Prothrombin Time (PT), Activated Partial Thromboplastin Time (aPTT), Thrombin Time (TT),
        b. Fibrinogen
        c. Activity of Factors II, V, VII, VIII, IX, X, XI, XII
        d. Activity of Protein C and Protein S
        e. Plasminogen, Antithrombin III (AT III), and α2-antiplasmin (plasmin inhibitor)
        f. pH, partial pressure of oxygen and carbon dioxide, sodium, potassium, chloride and osmolality
    2. Additives
        a. Chemical name
        b. Concentration in final product
        c. Total quantity in final product
        d. Purpose of additive
        e. Is the additive already FDA approved for use in humans?
    3. Sterility

iv. Pre-clinical test descriptions and results

v. Clinical test description and results

b. Maturity of manufacturing line:

i. Stage of development: bench top, third party manufacturer, pilot facility, regulated commercial production line

ii. Facility size and production capability

iii. cGMP compliant?
    1. Laboratory Assays
        a. Assay qualifications
        b. Assay validations
    2. Validated processes (for example)
        a. Raw materiel storage
        b. Intermediate product hold time(s)
        c. Equipment
        d. Clean rooms
        e. Lyophilizing
        f. Product transfer
        g. Packaging
        h. Cleaning
    3. In-process Controls/Specifications
    4. Release Specifications

iv. Is product produced on a manufacturing line that produces other FDA licensed or un-licensed products?
    1. Number of products manufactured on the line
    2. Product descriptions
    3. Process for transition between products
    4. Prevention of contamination

c. Development plan for product and manufacturing line:
    i. Description of commercial product (if different from current product)
    ii. Regulatory strategy
        1. Planned product testing
            a. Prior to IND
            b. Prior to BLA
        2. Manufacturing facility capital improvements
            a. Prior to IND
            b. Prior to BLA
        3. Planned manufacturing facility validation and documentation
            a. Prior to IND
            b. Prior to BLA
        4. Proposed clinical trials
    iii. Product development schedule through FDA licensure
        1. Gantt chart preferred
        2. Include all elements of the regulatory strategy
        3. Include times and resources required for each task
        4. Include all decision points and major milestones
    iv. Total budget
    v. Army funded
        1. Studies
        2. Budget
        3. Schedule (Gantt chart preferred)

EVALUATION CRITERIA:

1. Likelihood of commercial product to meet Army threshold (T)/objective (O) capability based on submitted data, product test results and development plan:
    - FDA approval (T=O),
    - no greater incidence of severe adverse events than currently experienced with fresh frozen plasma (FFP) (T), no adverse events (O),
    - Coagulation factor levels and other characteristics within the normal range for FFP (T=O),
    - no significant interactions with common operational drugs and vaccines (T), no interactions with any drugs or vaccines (O),
    - a portion (T) or all (O) of the supply must be universal donor,
    - reconstitution in less than 10 minutes (T) or 30 seconds (O),
    - unit size 200 ml glass container (T) or 250 ml ruggedized container (O), and
    - shelf life of one year when refrigerated between 1°C and 6°C (T) or stored between -20°C and +40°C (O)
2. Maturity of product and manufacturing line

3. Completeness and feasibility of development plan
4. Use/ leveraging of non-Army resources

Criteria 1 and 2 are of equal importance and are more important than 3 which is more important than 4. Cost is less important that the non-cost factors listed below.

SUBMISSION: **Pre-proposal submission deadline is 23 July 2007, at 12:00 pm EDT**. Please send pre-proposals in hard copy or electronic format and product samples to:

US Army Medical Research Acquisition Activity
ATTN: MCMR-AAA-06BAA/Aaron Wade
820 Chandler Street
Ft. Detrick, MD 21702-5014

Please contact USAMRAA prior to submitting your product by phone: 301-619-8397 or 301-619-2381, FAX: 301-619-6662 or Email: qa.baa@amedd.army.mil if the product requires special handling.

An e-mail will acknowledge receipt of your pre-proposal. Pre-proposals will be reviewed in order to identify proposals most likely to satisfy the Army's requirement. Invitations to submit a full proposal will be sent to the principal investigators whose pre-proposals are selected for further consideration. DO NOT submit a full proposal unless you receive a letter of invitation. Evaluation of the full proposal will include a manufacturing site visit. Performance periods should not exceed four years.

Anticipated Instrument Type(s): The USAMRMC implements its extramural research program predominantly through the award of grants and cooperative agreements. This award is expected to be a cooperative agreement. More information on these funding instruments may be obtained by request from USAMRAA at the above contact numbers.