AMENDMENT OF NIAID SOLICITATION

"In Vitro and Animal Models for Emerging Infectious Diseases and BioDefense"

Solicitation Number:	RFP NIH-NIAID-DMID-04-40
Amendment Number:	Two (2) (Q&A for Questions 1 – 27; 1st Posting)
Amendment Issue Date:	Wednesday, February 18, 2004
Proposal Due Date:	Tuesday, March 1, 2004 at 4:00 PM EST
Issued By:	Paul D. McFarlane Senior Contracting Officer NIAID, NIH, DHHS Contract Management Program, DEA 6700-B Rockledge Drive Room 2230, MSC 7612 Bethesda, Maryland 20892-7612
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Amendment Issued To:	All Potential Offerors

The hour and date for receipt of offers **HAS NOT BEEN EXTENDED**. Offerors shall acknowledge receipt of this amendment by noting, on the face page of the **original** technical and business proposals, that the offer has been prepared in accordance with the original solicitation and all its Amendments. Failure of the Offeror to submit this acknowledgement may result in the rejection of your offer.

PURPOSE OF AMENDMENT: I) To transmit to all Offerors the responses to Questions 1 – 27 that have been submitted concerning the solicitation; and II) To make changes to the Notes to Offerors, General Statement of Work for All Parts, Statement of Work for Part E, the Statement of Work for Sample Task Order E and the Instructions for Submission of Electronic Proposals.

I. THE FOLLOWING ANSWERS ARE BEING PROVIDED TO QUESTIONS THAT WE HAVE RECEIVED:
(**Note:** The responses to these questions do not change or otherwise affect this requirement except as indicated in Item II of this Amendment.

Question 1: Do you want detailed budgets (studies + travel) only for Year 1 or for Years 1 – 6? The appropriate escalation factor would be provided.

Answer: Your budget should include all of the costs associated with fulfilling the sample task order(s) for which you are submitting proposals. Therefore, if you are proposing a six-year study, the task order proposal(s) should include all the costs of performance for the six-year period.

Question 2: If we are to provide [a budget for] years 1 – 6, will there be a trip for the PI to Maryland each year or only in Year 1?

Answer: Actual task order awards will have an appropriate amount of travel specific to that task order. For the purposes of a general proposal to a sample task order, the assumption of one trip per year is provided for cost estimating purposes. (See revisions to Note #4 in Item II below).

Question 3: The basis for a detailed budget is clearly stated in [the] Statement of Work for Sample Task Order E. For the purpose of cost estimating, can we assume that the Sponsor will provide a method and kits for specific antibody determination?

Answer: Yes. If kits/methods are already developed, they will be provided. Note: the SOW allows for new assay development to be conducted under this contract, and in that case the reagents would not be provided. But for cost estimating purposes, it is reasonable to assume that methods/reference standards will be provided (see also revisions to the Statement of Work for Sample Task Order E in Item II below).

Question 4: We did not find a specific basis for the type of studies that required a budget preparation in [the Statement of Work for Sample] Task Order F. Would you provide the type of studies for budget purposes in order to make budget proposals uniform and compatible between the Offerors?

Answer: The Statement of Work for Sample Task Order F, Numbered Items 1and 2 are very clear and specific. Item Number 3 is subject to interpretation; however, for the purposes of this proposal, state whether you are proposing studies for a new compound **or** a FDA-approved antibiotic, as given in Paragraph 1. Items 4 and 5 are not likely to contribute significantly to cost and may be handled as indirect costs. As an example, FDA provides a draft guidance document for approved antibiotics seeking a label indication for inhalation anthrax:

http://www.fda.gov/cder/guidance/4848dft.htm

Question 5: There is a sentence starting at the bottom of the Background/Introduction section that says: "NIAID is limiting this reimbursement to $500,000 for Parts A, B, [C] and D." Can you please clarify whether the $500K is for each Part (Parts A-D) or [the] total for all four Parts?

Answer: This is the maximum reimbursement for equipment and renovation costs for each Part. Any renovation and equipment costs proposed must be associated with a specific task order award. You may propose renovation costs for any of the sample tasks for which you submit a technical and business proposal. The sample tasks, however, are not actual task orders. They are tasks that fit under each of the associated Parts. Proposing equipment and renovation costs as a part of a sample task order will require you to provide the appropriate scientific justification. The solicitation has been revised accordingly (see Item II below).

Successfully making the competitive range would not guarantee an Offeror's ability to obtain this funding unless an actual task order is awarded to your institution. Task orders may range from short duration, highly directed studies, to long term, labor intensive and evolving projects. Clearly, capacity factors into decisions on the part of both Offerors and the Government.

Question 6: How much weight will be given to whether an applicant has existing as opposed to pending Select Agent Registration (individual and facility)?

Answer: Select Agent registration is mandatory, but does not have to be met until the time of award, not necessarily at the time of proposal submission. Any specific information concerning the status of your Select Agent registration that is supplied in your proposal would be considered more favorably than general statements such as the "SA registration is in process."

Question 7: How many awards will be made [under] each Part in the RFP? I estimate there will be 20 to 30 awards for each Part. Is that true in the plan?

Answer: It is not possible, at this time, to forecast the number of awards that will be made for each Part. If an Offeror receives an award under more than one Part, only one contract document will be executed that includes all Parts awarded under the solicitation. We anticipate making approximately 5 – 10 contract awards under this solicitation. The number of contract awards, however, will depend on available funding and the needs of the NIAID.

Question 8: I [have] seen the brief information regarding NIH-NIAID-DMID-04-40 and noted the statement: "For Parts C, D, E and F, various vaccine concepts may be tested based on the following categories: (a) synthetic peptides, (b) recombinant subunits, (c) vector-based vaccines, (d) virus-like particles/replicons, or (e) nucleic acid."

I am not clear if this 04-40 would provide a contract to advance and further test a recombinant subunit display and delivery system …or, whether it merely is soliciting contract proposals to provide testing services if you will for accessing various vaccine concepts which have been put forth or are being developed by others.

Answer: The intent of this program is first to secure the testing services. NIAID already has some advanced products in the pipeline utilizing these services. However, once set up, the infrastructure could be used for other products in the future and mechanisms to get those products will be explored at a later time.

Question 9: Will the award winner in [DMID-]03-39 be precluded from bidding on [DMID-]04-40?

Answer: Current Contractors may choose to submit task order proposals to compete for Parts under this solicitation for which they did not receive contract awards under [DMID-]03-39.

Question 10: Toward the end of the General Statement of Work For All Parts, in the paragraph preceding the information for Part A, the "Safety Controls and Standards" mentioned indicates that it is attached to the document. I am unable to locate this attachment on the web site with this RFP or when I do a search of the site. Where can I find a copy of this information?

Answer: References to this clause have been deleted from the solicitation as a part of this Amendment. (Please see Item II below).

Question 11: Reference is made to FAR 52.227-11, Patent Rights-Retention by the Contractor (Short Form) (June 1989). Should this reference instead be the subject FAR clause dated June 1997?

Answer: Yes. The date for this clause has been revised as a part of this Amendment (please see Item II below).

Question 12: The proposed contract is expected to be indefinite-delivery, indefinite-quantity with guaranteed minimum dollar awards for each awarded Part. Since there is no guarantee that Offerors will receive more than $500,000 in task order work over the entire period of performance, and they could only receive the guaranteed minimum, is a Small Business Subcontracting Plan required with the initial submittal of a proposal in response to the solicitation and, if yes, is the cost basis for determining planned subcontracting dollars the guaranteed minimum for each Part?

Answer: We are requesting master subcontracting plans for the entire contract period based on the ceiling amount of the contract(s) which will be $80M. The submission of this plan should be in accordance with the instructions contained in the solicitation.

Question 13: Is membership in NCCLS required?

Answer: No, it is not required. It does, however, represent the industry standard, particularly for Part B.

Question 14: Our institution is one that was awarded....and much of the work that we are proposing (particularly the GLP work) is to be done in that laboratory. Construction of the lab is not due to be complete until the end of 2005. Is it alright to propose the GLP work [in that lab] even though it is not built?

Answer: Yes. Any information you can provide about the progress on the lab's construction will be helpful.

Question 15: How much detail is needed for a plan to achieve GLP compliance? Do I need SOPs or can I describe what we will do to achieve GLP and provide a timeline for this?

Answer: Obviously, the more detail you provide about your plans, the better NIAID will be able to assess the feasibility/appropriateness of the plan. It often takes some time to achieve GLP compliance, and the more work that is done by the time of proposal submission, the easier it is for NIAID to gauge your level of readiness. However, even a preliminary plan will give NIAID something to assess. We recognize that SOPs for a facility that is not yet built or renovated will be difficult to produce at this time.

Question 16: Are the minimal award values for direct costs or total costs?

Answer: Total Costs.

Question 17: We are applying for 4 Parts…. For the structure of the technical proposal, can we write one general section of background information that applies to all the Parts or should we envision that the technical proposal will be divided up and given to different reviewers for each Part, hence, each Part should be a complete proposal that can stand alone?

Answer: You must submit a separate, stand alone sample task order proposal for each Part for which you propose. However, language that is applicable to all Parts can simply be reproduced in each proposal.

Question 18: For [a] sample task order proposal, do we include a budget?

Answer: Yes, you should include all of the costs of performance associated with the task order.

Question 19: In Note #4 of the General Statement of Work [for all Parts], it says to plan for one person to travel to Washington once per year. Is this one person per Part or one person for the whole thing?

Answer: See response to Question #2 above.

Question 20: Are the general statement of work, statement of work for the different Parts (A, C, E and F in our case) and the sample task orders (for the four different Parts) all to fall within 150 pages?

Answer: The page limitation is per task order proposal submitted. The solicitation has been revised accordingly (see Item II below).

Question 21: Can you provide a rough idea of the percentage of the total contract funding that will be applied to Parts A and B?

Answer: It is not possible to predict this amount at this time.

Question 22: Once compounds or strains are sent to a company, what is your desired turnaround time?

Answer: You can base your turn-around time on the pathogen under investigation.

Question 23: Once a company is selected as a source for screening, can the list of pathogens be later expanded?

Answer: Yes, with additional task orders or modifications to existing task orders.

Question 24: Can we propose our services initially for BL2 pathogens until that time when investment in a BL3 facility upgrade makes financial sense?

Answer: Yes.

Question 25: If you were preparing a proposal as a cash-strapped startup, would you emphasize the flexibility afforded small organizations and propose all capabilities (within the spectrum of demonstrated skills) or would you focus on 1-2 organisms?

Answer: Focus on your strengths.

Question 26: I expect [we] would need to generate roughly $500,000/year of revenue to make this venture feasible. Is this amount within the reasonable range of expectation?

Answer: Only the minimum amounts for each Part are guaranteed.

Question 27: What level of physical security is required for facilities stocking these organisms? Will [we] be required to place alarms on the storage freezers? Will we be required to hire fulltime security guards? Will we be required to provide background checks and security clearances for all personnel?

Answer: Every offeror must be registered and abide by Select Agent rules. For more information please go to: http://www.cdc.gov/od/sap/.

II. THE FOLLOWING CHANGES ARE HEREBY MADE TO THE SOLICITATION:

Section A – Solicitation/Contract Form

The telephone number of the Contract Specialist on page 1 of the solicitation is hereby corrected from "(301) 351-3692" to "(301) 451-3692."

Introduction

The second paragraph of this section, page 7, bottom of page, is hereby revised to clarify the maximum reimbursement for equipment and renovations of contractors' facilities. This sentence is changed to read as follows: "NIAID is limiting this reimbursement to $500,000 per Part for Parts "A, B, C and D."

Awards Made Under NIH-NIAID-DMID-03-39

The award information for Southern Research Institute is hereby revised to show the correct Parts awarded under DMID-03-39. The correct Parts were: "A, B, C and D."

General Statement Of Work For All Parts

All references to the Safety Controls and Standards found in this section and throughout the solicitation are hereby deleted.

Statement of Work for Part E: Safety/Toxicology and Immunogenicity Testing for Vaccines

The Part E Statement of Work is being revised to add testing of human samples employing the assays used for animal studies, with modification if necessary. This results in the following additions to the SOW:

- Add the following sentence to the end of the 1st paragraph in the statement of work: "In many cases the same or modified versions of assays used to test animal sera or cells will be employed to analyze human samples from clinical trials."

- Renumber Item #2 as Item #3 and add the following Item #2: "Clinical immunogenicity testing: The Contractor may be asked to test samples from clinical studies designed to assess the immune response in humans, including antibody levels and subtype, and cell mediated immune responses. Testing of human samples derived from clinical trials must be conducted under Good Laboratory Practices (GLP) and with validated assays. Clinical testing may include but is not limited to the following:

    a. Determination of humoral responses.
    b. Antibody quantitation and sub-typing.
    c. Determination of antigen-specific immune responses.
    d. Determination of neutralizing antibody activity.
    e. Assessment of T-cell immunity."

A revised Statement of Work for Part E is provided as Attachment A to this Amendment. All changes have been highlighted.

Notes to Offerors: General Statement of Work for All Parts

Note #3 is hereby revised to change the last sentence of this note to: "(See the attached HHS Safety and Health clause and Item #5 of the General Statement of Work.)" The following information is also added to this note: "Links for current, relevant safety documents can be found at: http://www.nih.gov/od/ors/ds/pubs/.

Note #4, last sentence, is hereby revised to read: "For the purpose of preparing a business proposal, assume one visit of one key personnel per task order per year to Bethesda, MD to meet with the Project Officer and other DMID personnel.]"

Note #5 is hereby revised to change the date for FAR Clause 52.227-11 – Patent Rights-Retention by the Contractor (Short Form) from "(June 1989)" to "(June 1997)".

Statement of Work for Sample Task Order E: Safety and Immunogenicity Testing for Vaccines

Paragraph 3 of Note #1 to Sample Task Order E is hereby revised to add the following information:

"For the purposes of a preparing a business proposal, guidance on the number of human samples for possible vaccines are as follows:

For recombinant Protective Antigen (rPA) anthrax vaccine, Offerors should provide capabilities (throughput, infrastructure, equipment and expertise) and proposed budget to assay 3,000 human samples by ELISA and 1500 samples by TNA. Samples will be analyzed in duplicate. Thus, a total of 6,000 ELISA assays and 3,000 TNA assays including repeats are estimated. Assume that samples will be sent in batches of 500-600.

For Modified Vaccinia Ankara (MVA) vaccine, Offerors should provide capabilities (throughput, infrastructure, equipment and expertise) and proposed budget to assay 3,500 human samples by vaccinia virus neutralization and ELISPOT assays. Samples will be analyzed in duplicate, thus 7,000 virus neutralization and 7,000 ELISPOT assays per year. Assume that samples will be sent in batches of 500-600."

A revised Statement of Work for Sample Task Order E is provided as Attachment B to this Amendment. All changes have been highlighted.

Packaging/Delivery/Electronic Submission of Proposal

The following information is being provided to clarify the submission instructions for the task order technical proposals and task order business proposals that must be submitted in response to Parts A – F of the solicitation:

A separate task order technical proposal and a separate task order business proposal must be submitted for each Part of the solicitation for which you wish to submit a proposal in an original and 15 copies (see Amendment #1 to the solicitation). Each task order proposal must be a separate, stand alone document that can be evaluated independently of any other proposal submitted for any other Part of the solicitation. All information that you wish to have considered in the evaluation of your proposal must be contained in your technical and business proposals for that Part of the solicitation. The page limitation of 150 pages is per sample task order proposal (technical) submitted.

Due to the amount of interest expressed in this solicitation, Offerors will not be required to submit proposals electronically through CRON (Contracts Review Online). Instead, you must submit your proposal(s) on a CD-ROM or ZipDisk along with the paper copy of your proposal. An electronic copy of your proposal(s) will then be uploaded electronically by our office to CRON. **You must certify that the original paper and electronic versions of your proposal(s) are identical by placing a statement on the cover page of each "original" technical and business task order proposal.**

STATEMENT OF WORK for PART E: SAFETY/TOXICOLOGY AND IMMUNOGENICITY TESTING for VACCINES

The fifth activity area to be supported under this contract is the testing of vaccine preparations as required prior and subsequent to initial clinical evaluation. This includes preclinical testing of candidate products for safety and immunogenicity (both cellular and humoral) in small animals and, if appropriate, in non-human primates. In many cases, the same or modified versions of assays used to test animal sera or cells will be employed to analyze human samples from clinical trials.

Independently, and not as an agent of the Government, the Contractor shall test candidate products for safety and immunogenicity (both cellular and humoral) in small animals and in non-human primates, and other appropriate tests, including reproductive toxicology in animals. Perform all such tests as are required to support clinical use in humans of a vaccine product, which may include testing of human samples derived from clinical trials conducted elsewhere. Testing must be sufficient to meet requirements for IND filing.

Specifically, the Contractor shall:

1. At the request of the Project Officer, the Contractor shall perform all tests required to qualify a vaccine product for human administration or to qualify relevant cell substrates for vaccine production, or to evaluate human and animal samples including but not limited to the list below. Such testing must also include assays required to support Investigational New Drug (IND) and Masterfile submission and updates. All studies must be performed in accordance with GLP regulations (21 CFR 58) unless otherwise specified by the Project Officer in writing.

a. Preclinical immunogenicity evaluation: The preclinical studies shall be designed to assess the immune response including seroconversion rates, antibody levels, and cell mediated immune responses in vaccinated animals.

b. Preclinical safety evaluations shall include but are not limited to the following:

1) Systemic toxicity: Preclinical studies shall include dose-ranging and dose escalation studies of systemic toxicity as well as toxicity to potential target organs, including hematopoietic and immune systems, and histological evaluation of organs.

2) Local reactogenicity: Local site reactivity studies to include detailed clinical observations and histological evaluation of tissue at the injection site or other visible lesions from biopsies or term necropsy samples.

3) Genetic toxicity: In the case of DNA and vector-based vaccines, the pivotal GLP preclinical study shall focus on assessment for the potential for the nucleic acid vaccine to first spread within the host, and second to recombine with endogenous host DNA sequences and integrate into cell chromosomes. Studies designed to address the potential for biodistribution and integration shall use the most sensitive methods available.

4) Tumorigenicity studies: Tumorigenicity studies may be appropriate under certain conditions, such as if the preclinical genetic testing demonstrates evidence of integration activity and/or broad tissue distribution, or to qualify cell substrates used in vaccine production. Such studies shall be performed when necessary.

5) Reproductive toxicity studies: Reproductive toxicity studies must be performed prior to the use of these vaccines in pregnant women. Such studies shall include but are not limited to fertility, general reproductive performance, teratology, and developmental toxicity.

6) All other safety tests as may be required for a particular vaccine type.

c. Adjuvant testing: The use of adjuvants and/or facilitators for the administration of a vaccine will necessitate specific preclinical evaluation procedures to ensure the safety of the candidate formulation to include but not limited to the evaluations listed in b) above.

2. Clinical immunogenicity testing: The Contractor may be asked to test samples from clinical studies designed to assess the immune response in humans, including antibody levels and subtype, and cell mediated immune responses. Testing of human samples derived from clinical trials must be conducted under Good Laboratory Practice (GLP) and with validated assays. Clinical testing may include but is not limited to the following:

a. Determination of humoral responses.
b. Antibody quantitation and sub-typing.
c. Determination of antigen-specific immune responses.
d. Determination of neutralizing antibody activity.
e. Assessment of T-cell immunity.

3. In addition, the Contractor shall:

a. Provide all data, information, and records required for the writing and submission of the Masterfile, Investigators Brochure, and all other documents related to IND submission and maintenance to the Project Officer or to a designated third party.

b. Retain all records, samples, histopathological slides, etc. and make them available as directed by the Project Officer and as indicated under GLP guidelines.

c. Maintain awareness of evolving regulatory requirements for preclinical immunogenicity and safety evaluations for vaccines, and develop new test systems or models as required to meet new needs.

d. Acquire, validate, and utilize assay/organism-specific standardized reagents and controls to the extent possible.

e. Participate as necessary in discussions with the FDA during pre-IND, IND, and pre-NDA meetings.

4. Meet all items outlined in the General Statement of Work for *In Vitro* and Animal Models for Biodefense and Emerging Diseases.

STATEMENT OF WORK for SAMPLE TASK ORDER E
SAFETY AND IMMUNOGENICITY TESTING FOR VACCINES

The activity to be supported under this contract is the testing of vaccine, such as (a) synthetic peptides, (b) recombinant subunits, (c) vector based vaccines, (d) virus-like particles/replicons, or (e) nucleic acid based vaccines), as required prior to, or during, clinical evaluation and for continued clinical development. This includes testing candidate products for safety and immunogenicity (both cellular and humoral) in animals and humans.

[NOTE #1 to Offerors: Include all testing required for an IND and for advanced clinical development (Phase II trials and including special populations) for this type of product. The proposal should be structured in terms of specific milestones to be accomplished. Reports will be provided upon completion of each milestone. Provide a timeline. The Government will provide the test vaccine.

Offerors who have the capability to perform the studies in accordance with GLP shall do so. Those who do not may propose to do the studies but should clearly include a plan for achieving GLP compliance. The Offeror should clearly identify the types of animal(s) that will be used in each study.

For the purposes of providing a business proposal, Offeror(s) should provide a detailed budget based on the preclinical and/or clinical safety and immunogenicity evaluation of one vaccine product. Assume that tumorigenicity and reproductive toxicity studies are not required for the cost estimate. Include documentation for personnel costs and all specific animal, supply, and equipment costs. For the purposes of preparing a business proposal, guidance on the number of human samples for possible vaccines is as follows:

For recombinant Protective Antigen (rPA) anthrax vaccine, offerors should provide capabilities (throughput, infrastructure, equipment and expertise) and proposed budget to assay 3,000 human samples by ELISA and 1500 samples by TNA. Samples will be analyzed in duplicate. Thus, a total of 6,000 ELISA assays and 3,000 TNA assays including repeats are estimated. Assume that samples will be sent in batches of 500-600.
For Modified Vaccinia Ankara (MVA) vaccine, offerors should provide capabilities (throughput, infrastructure, equipment and expertise) and proposed budget to assay 3,500 human samples by vaccinia virus neutralization and ELISPOT assays. Samples will be analyzed in duplicate, thus 7,000 virus neutralization and 7,000 ELISPOT assays per year. Assume that samples will be sent in batches of 500-600.]

1. Specifically, the Contractor shall perform all tests to qualify a vaccine product for human administration including but not limited to the list below. Such testing must also include all tests required for Investigational New Drug (IND) and Masterfile submissions and maintenance. In addition, include all testing that will be necessary to expand clinical development to special populations. All studies must be performed in accordance with Good Laboratory Practice (GLP) regulations (21 CFR 58).

a. Preclinical immunogenicity evaluation: The preclinical studies shall be designed to assess the immune response including seroconversion rates, antibody levels, and cell mediated immune responses in vaccinated animals. Studies should also be designed to establish a model for determining potency.

b. Preclinical safety evaluations may include but are not limited to the following:

1) Systemic toxicity: Preclinical studies shall include dose ranging and dose escalation studies of systemic toxicity as well as toxicity to potential target organs including hematopoietic and immune systems.

2) Local reactogenicity: Local site reactivity studies to include detailed clinical observations and histological evaluations of tissue of the injection site or other visible lesions from biopsies or term necropsy samples.

3) All other safety tests as may be required for a particular vaccine type and for advanced clinical development, such as genetic toxicity, tumorigenicity, and reproductive toxicity studies.

2. Clinical immunogenicity evaluation: The preclinical studies shall be designed to assess the immune response including seroconversion rates, antibody levels, and cell mediated immune responses in vaccinated humans.

3. Provide all data, information, and records required to support regulatory filings to the Project officer or to a designated third party. This information shall be submitted within three weeks of the time the Project Officer makes the request.

4. Complete all tasks as outlined in the General Statement of Work for *In Vitro* and Animal Models for Biodefense and emerging diseases and the Part E Statement of Work.

NOTES

[NOTE #E-1 TO OFFERORS: Documentation of experience in preclinical safety and evaluation of immune response testing should be provided. It is anticipated that the contractor will have the capacity to perform testing for each type of vaccine candidate covered by this contract, including each of the four general vaccine Categories. Offeror should outline in detail the tests and procedures it will use to qualify each type of vaccine product for human administration. Provide an appropriate model for determining the cellular and humoral immunogenicity of vaccine in small animals and, if necessary, in non-human primates. Offeror(s) should provide documentation of models/protocols that have been used successfully in previous investigations. Offeror(s) may propose subcontracts for any specific testing procedure (e.g., primate studies). Documentation of available equipment and access to an AAALAC-accredited (or equivalent) animal facility and the capacity for testing the safety and immunogenicity of products should be included.]

[NOTE #E-2 TO OFFERORS. Specific requirements listed in the Statement of Work are not meant to limit the scope or specifics of preclinical vaccine testing. Such testing will include all of the tests required to qualify a vaccine product for human administration.]

[NOTE #E-3 TO OFFERORS. In addition to the CFR, the FDA also provides "Points to Consider" (PTC) Documents. Testing should be conducted consistent with these guidelines. Examples of relevant guidelines include:

a) Points to consider in the Production and Testing of New Drugs and Biological Produced by Recombinant DNA Technology (4/10/85). Supplement (4/6/92).
b) Points to Consider in Human Somatic Cell Therapy and Gene Therapy (8/29/91).
c) Points to Consider in the Characterization of Cell Lines Used to Produce Biologicals (7/12/93).
d) Points to Consider for Plasmid DNA Vaccines for Preventive Infectious Disease Indications (10/96)

These documents, as well as additional guidelines relating to testing and manufacture, are available from the Division of Congressional and Public Affairs. To receive copies call 888-223-7329 then dial 999 to get a list of documents and their number. Consumer information number is 301-827-2000. On the Internet go to http://www.fda.gov/cber/.]