

**Office of Research and Development Coordination**  
**RFP-DHHS-ORDC-V&B-05-08 – AMENDMENT No. 2**  
**Advanced Development of Antigen Sparing Pandemic Influenza**  
**Vaccines**

**Technical and Business Questions and Responses -**

1. The RFP permits manufacturing at a foreign site if the product has long-term stability data such that the product is suitable for stockpiling at an FDA-licensed facility in the US. Can HHS provide guidance on what type of long-term stability data will be suitable to permit product produced outside of the US to be stockpiled within the US? For example, for what time period must stability be demonstrated?

**A1. Comparability to licensed influenza antiviral drug products such as oseltamivir phosphate – 5 years – would be a reasonable expectation.**

2. Can Phase III costs for a novel adjuvant containing cell-culture pandemic vaccine, originally developed under RFP-DHHS-ORDC-V&B-05-04, be reimbursed under this antigen sparing RFP, particularly if the CC-Pan vaccine is sufficiently different from the CC-TIV such that a separate license is required?

**A2. Adjuvant strategies developed for cell-based pandemic vaccines in response to RFP ORDC V&B 05-04 are expected to be the best that the Offerors have. This solicitation does not provide funding to the alternative or secondary adjuvant approached not proposed in the other RFP.**

3. What will be the criteria to define what is a potent dose of H5N1 vaccine? Will it be the CHMP criteria or some other criteria?

**A3. Criteria used to define potency of H5N1 vaccine products is the SRID assay results. If potency is used in this context to mean protective, then please refer to the recent study (Treanor *et al.* 2006, NEJM) using an egg-based inactivated H5N1 vaccine in humans for guidance on clinical endpoints.**

4. What type of "firm commitment" is HHS anticipating regarding the establishment of facilities capable of producing 150 million doses for stockpile within 6 months of US licensure?

**A4. The technical proposal must state that the Offeror will commit to building a vaccine manufacturing facility in the U.S. if awarded the contract and the product is shown to be safe and efficacious. Milestones 3 and 4 (Facility and Feasibility Plans) provide the framework and basis for the establishment of the vaccine manufacturing facilities.**

5. The manufacturing capacity will obviously be greatly affected by the yield and effectiveness of antigen sparing technologies which are uncertain at this time. In light of that, how should bidders assess the likelihood of satisfying the 150 million dose commitment? Should this be calculated based on a certain assumed antigen content (e.g. can we presume a dose of 3.8 mcg)?

**A5. Assumptions on the amount of antigen must be based on data generated in appropriate animal models and human clinical trial results available in the public domain as published results or that is proprietary to the Offerors or its Subcontractors.**

6. Would a firm commitment of 150 million doses be considered responsive if the bid was based on an assumption that a 3.8 mcg dose was immunogenic, with clinical trials to be conducted early in the contract term to confirm this assumption? What would happen if those clinical trials ultimately demonstrated that a 3.8 mcg dose was insufficient, thereby resulting in a capacity of less than 150 million doses?

**A6. Assumptions must be made on sound scientific data as stated above in A5. If the assumptions are proven incorrect, then the proposal should provide alternate critical pathways and the commensurate timelines and costs to achieve the mandatory requirement of 150 million doses in six (6) months. The usage of decision-trees in the critical pathway for product development would be useful to illustrate these avenues of choices.**

7. If a bidder has a preexisting supply agreement with another national government, may the commitment to supply 150 million doses within 6 months of licensure be subject to that preexisting commitment? Would HHS be willing to consider a proposal that provided a firm commitment of less than 150 million doses if a bidder had a preexisting contractual commitment to another government?

**A7. The proposal should state how the Offeror is able to meet this capacity requirement in fulfillment of this contract and is not subject to terms of other Agreements that the Offeror may have or will have.**

8. Will HHS be committed to purchasing 150 million doses for stockpile from a successful bidder? If not, what are the limitations on a bidder engaging in discussions or commitments to stockpile for other governments?

**A8. This solicitation provided support for the advanced development of antigen-sparing pandemic influenza vaccines towards U.S. licensure. For providing significant funding of these product development costs, HHS requires a commitment to establish a U.S. facility for vaccine manufacturing or demonstration that a product may be stockpiled rapidly in sufficient quantity. This is not an acquisition contract for vaccine. Contracts awarded in response to this solicitation do not preclude Contractors from making commitment to others. However, if such**

**commitments jeopardize the surge capacity for the U.S. supply, then the contract may be terminated.**

9. Assume a company submitting a bid on this Antigen Sparing RFP was also awarded a contract for RFP-DHHS-ORDC-V&B-05-04 (the cell culture RFP), which required that a company establish a US based manufacturing surge of capacity of 150 million doses within 6 months, and assume further that the cell culture candidate vaccine was an antigen sparing adjuvanted cell culture vaccine. Assuming such facts, does the antigen sparing adjuvanted cell culture capacity under the cell culture contract also satisfy the capacity requirement under the antigen sparing RFP, or is the capacity requirement for the antigen sparing RFP incremental to cell culture capacity?

**A9. Yes, but Offeror can not be funded for the same work with contracts from each of these solicitations.**

10. Page 5 of the RFP states that the purpose of this RFP is "to support advanced stage development of enhanced immunity and/or antigen-sparing strategies for pandemic influenza vaccination..." Please define "advanced stage of development".

**A10. Advanced stage development refers to clinical manufacturing & evaluation, mfg process and scale-up development for commercial scale manufacturing of the product.**

11. Does this RFP only support development activities designed to lead to licensure for a pandemic vaccine, or does DHHS also anticipate that inter-pandemic licensure should result from activities funded under this RFP?

**A11. RFP supports development of dose-sparing products or approaches for pandemic vaccine usage.**

12. On page 52 of the RFP, under the Technical Evaluation Criteria for Facilities, there is a discussion of the required facility capacity, depending on whether a product can be stockpiled or not (300M vs. 150M in 6 months). What is HHS' preferred option: (1) to have a facility able to produce 150M doses within 6 months or (2) to have a 300M dose stockpile?

**A12. 150 million doses in six months.**

13. Is it within the scope of this RFP to submit a proposal that supports the development of an adjuvanted pandemic influenza vaccine that is being developed through Phase 2 clinical trials under a separate procurement? In other words, would a proposal be compliant with this RFP that encompasses the performance of Phase 3 clinical trials in all populations and the submission of a Biologics License Application (BLA) for a pandemic influenza vaccine that is being taken through Phase 2 clinical trials under a separate procurement?

**A13. Studies being supported by other U.S. Government contracts or grants can provide supportive data for a proposal for this RFP, however a contract awarded from this RFP can not be used to support studies previously funded. If the studies are separate or a continuation of previously USG-funded studies, then the newly proposed studies may be considered for funding under this RFP.**

14. Please clarify the Objective (c) listed on page 6 of the RFP. It is our understanding that if a product has extended long-term stability (i.e., 2 years or more), and subsequently is suitable for stockpiling in the U.S. at an FDA-licensed facility, that the product can be produced in a facility outside of the U.S. This facility must have the capacity to support rapid stockpile purchases commensurate with U.S. pandemic influenza vaccine needs, but we understand Objective (c) to mean that the facility need not be located in the U.S. as long as the product is suitable for stockpiling in the U.S. Please confirm our understanding of this objective.

**A14. The mfg facility may be located abroad provided that sufficient surge capacity is documented and confirmed for stockpiling purposes.**

15. Does the DHHS anticipate that the Food and Drug Administration (FDA) will release draft guidance related to antigen sparing pandemic influenza vaccines? DVC has used the Draft Guidance that the FDA released related to pandemic vaccines, but we are not aware of any guidance, planned or released, that is specific to antigen sparing technologies. DVC strives to utilize all current available guidance from the FDA in formulating our regulatory and product development strategies; subsequently, if the DHHS is aware of future guidance that can be expected from the FDA, this information would be helpful in formulating our proposal in response to the RFP to ensure that our strategy best meets the requirements of the DHHS in support of the pandemic preparedness program.

**A15. FDA has provided pandemic vaccine guidance documents within the last 30 days. Please see the CBER/FDA website.**

A copy of the guidance, "Draft Guidance for Industry, Clinical Data Needed to Support the Licensure of Trivalent Inactivated Influenza Vaccines," is available at:  
<http://www.fda.gov/cber/gdlns/trifluvac.pdf>.

A copy of the guidance, "Draft Guidance for Industry, Clinical Data Needed to Support the Licensure of Pandemic Influenza Vaccines," is available at:  
<http://www.fda.gov/cber/gdlns/panfluvac.pdf>.

16. Does this RFP only support development activities designed to lead to licensure for a pandemic vaccine, or does DHHS also anticipate that inter-pandemic licensure should result from activities funded under this RFP?

**A16. HHS Response: This RFP may support developmental activities leading to licensure depending on the design of the studies proposed.**

17. Would you please confirm that this RFP could support activities leading to licensure of an inter-pandemic vaccine?

**A17. This RFP supports activities supporting the licensure of pandemic influenza vaccines towards U.S. licensure not seasonal influenza vaccines per se. However there are many crossover activities between the two vaccines that could be considered for support.**

18. Regarding Mandatory Criteria #2a, found on page 50 of the RFP, shown below. Our interpretation is that in the case of an adjuvanted vaccine, the reference to "product" refers to the final formulated adjuvanted vaccine. Please confirm.

**A18. Final container product is acceptable if the product is pre-formulated. If product is used at patient's bedside with antigen, then, the adjuvant product alone is used. If product is a medical device, then the final product is the device that is used with the final container vaccine product.**

19. Given the ongoing threat of an influenza pandemic, it is essential that efforts funded as a result of this requirement shall lead to U.S. licensure of an influenza vaccine and/or delivery system that can be used to protect the U.S. population in the event of an influenza pandemic. Therefore, Offerors must commit to the following to be considered for award:

(a) Agreement to submit the **product** to HHS for side-by-side comparison with other different antigen-sparing pandemic vaccine approaches for assessment of their relative capabilities in a standardized animal and/or clinical trial.

**A19. Yes.**

20. Will pre-award costs be eligible for reimbursement?

**A20. All direct costs charged to a resultant contract must occur either during the contract period of performance or in accordance with the cost principle in FAR 31.205-32 Pre-contract Costs.**

21. We would like to present labor effort and costs for RFP-DHHS-ORDC-V&B-05-04 using pools of personnel (hereafter referred to as the Labor Categories method). This method is in lieu of using an Employee Name based method, which lists actual personnel who would potentially perform on the contract at some future time. The Labor Categories method is in agreement with the Personnel Cost Format instructions on page 37 of the RFP section 3a which states: "If a pool of personnel is proposed, list the composition of the pool and how the cost proposed was calculated". Subsequently, we plan to propose effort by labor categories.

The categories will consist of the current employees assigned to each job title and grade level. Our HR department, who developed these job titles and levels, will

calculate an average labor rate (hourly rate) for each category. The HR department relies on several compensation surveys to develop these models and the models are updated on an annual basis. In addition, similar information is generated for each country.

**A21. An offeror can propose labor/effort costs as outlined in the RFP. Please be aware that proposals submitted in response to this RFP will require cost analyses and/or audits of each element of cost proposed. Offerors will be required to submit supporting documentation to verify the accuracy of all proposed costs, no matter what the manner of presentation. Further information concerning the requirements for Cost or Pricing data is located in the RFP under Section L, Item 24.**

22. How should the technical proposal content be organized?

**A22. See sections I, L, and M of the RFP for instructions and guidance.**

23. Besides the budget summary page, what is the requirement for budget detail that needs to be provided and is there a preferred format?

**A23. See Section I and pp. 36-37 for business proposal format. This amendment also contains a summary of proposed costs template in excel format.**

24. Can renovation costs to an existing building or manufacturing facility, such as enhanced air handling and water systems, be covered under this RFP? Our intent is to submit a proposal that utilizes a modular design for antigen production. Does this RFP cover the cost of a module(s)?

**A24. No.**

25. Will the manufacturer of a pandemic flu vaccine receive indemnification under the legal authority as outlined in the HHS Pandemic Flu plan?

**A25. Liability immunity is provided by Statue under Public Law 109.148 – PREP Act of 2005 upon declaration of a public emergency by the Secretary of Health and Human Services.**

26. Is it acceptable to manufacture pilot GMP bulk antigen for early clinical trials (phase I and phase IIa) outside of the US (e.g., in UK) for fill/finish in the U.S.?

**A26. Yes.**

27. What are the Agency's thoughts on the fate of validation lots?

**A27. This question should be posed to FDA directly.**

28. Since the exact extent of the antigen sparing effect will not be known until after the initial clinical trials, manufacturing cost for scale production of 150 million doses in 6 months will be difficult to accurately budget. What is the Agency's position on contract adjustments?

**A28. Eligible projects should be far enough along to provide supportive data on production estimates. Since this RFP does fund the establishment of manufacturing facilities, then results of dose ranging studies (Phase I) should be available within the first year of the contract and should not affect the cost of preparing pilot lots and clinical studies.**

29. If the Company fulfills the contract, can a future procurement of pandemic vaccine be expected from HHS?

**A29. HHS will consider many options including dose-sparing in achieving adequate pandemic vaccine production.**

30. This is a fee based program. Is there federal guidance related to fee structure? Is it necessary to break the fee out of any given line item charge or can it be incorporated?

**A30. No it is not necessary to break out profit/fee for any given line item charge. Any proposed profit/fee should be presented in total and in accordance with the offerors cost/pricing policies. See FAR 15.404-4 Profit, for the Government's guidance on cost analysis of profit.**

31. Will the Department make vaccines developed under contract to the U.S. Government available to companies selected as a result of this solicitation for animal and clinical testing of the antigen-sparing products? Should potential Offeror's plans for animal and clinical testing of their antigen-sparing product anticipate testing with vaccines funded by the government?

**A31. No, procurement of antigen is Offeror's responsibility**

32. Please provide the Department's definition of long term stockpiling. Is this anticipated to be 6 months? One Year? Two Years? Some other time period?

**A32. HHS will establish and maintain stockpiles of vaccines and other supplies that may be necessary in a pandemic and will reevaluate the status of the stockpiles periodically as needed. Many SNS products have shelf lives of 3-5 years.**

33. Milestone 3, items A., B. and C. (RFP pages 7-8) all require a production plan for 150 million doses within a 6 month period. However, in Section M.3. Technical Evaluation Criteria, 3. Facilities, (b) a requirement for 300 million units in 6 months for products with long-term stability suitable for stockpiling is given.

**A33. 150 million doses in 6 months is correct value.**

34. First, what shelf life (in years) is considered suitable for stockpiling?

**A34. See A32.**

35. For products with long-term stability suitable for stockpiling, which capacity is required, that indicated in Milestone 3 C. (150 million doses) or M.3.3. (b) (300 million doses) in a 6 month period?

**A35. See A33.**

36. Under Objectives on Page 6, activities that may be supported include product dedicated manufacturing equipment, process validation, and facility validation. However, in order to assign accurate budgetary costs to these activities the Contractor would first have to complete Milestone 3.D., essentially identifying and specifying the equipment required to achieve the desired capacity.

**A36. If the Offeror is not far enough along in the development of the product, then this RFP may not be operative for their Program.**

37. For purposes of the proposal, will it be sufficient to estimate the equipment and validation costs (e.g., order-of-magnitude) likely to be incurred based on the current status of the manufacturing process, subject to revision once the detailed process scale-up and equipment specification have been completed in Milestone 3.D.?

**A37. See A36. Otherwise the best estimates are considered and may be considered as cost ceilings for future contract modifications.**

38. In the RFP (Background, p5) the government indicates “Strategies that can be implemented by influenza vaccine manufacturers worldwide rather than being tied to a specific manufacturer or product would be most advantageous”.

Licensure of an Antigen Sparing technology for use with influenza vaccine produced by multiple vaccine manufacturers may require clinical testing with influenza vaccine produced by multiple vaccine manufacturers. Ideally, such studies would require access to clinical grade vaccine produced by the suppliers selected by the government.

**A38. We are not clear on what is the question; however, the statement (background, p5) relates to products that may be used with different influenza vaccines. It does prohibit or discourage collaborative arrangements for the product development with a given influenza vaccine.**

39. As these comparative clinical studies would be required for licensure, should they be included in the clinical and regulatory plans?

- a) Would the HHS sponsor and manage the comparison studies required for licensure of an Antigen Sparing technology for use with multiple pandemic influenza vaccines?
- b) Would the HHS provide the different vaccine preparations required to support the comparative studies and rely on the offeror to perform the studies under HHS sponsorship?
- c) Should projected costs associated with at least one such comparative study be included in the cost proposal?

**A39. No, HHS will perform these evaluations. The Offeror will provide the product and/or assist in its formulation with HHS selected antigen(s).**

40. Which (if any) of the following documents/forms are to be counted toward the 40 page maximum for the technical proposal? Technical Proposal Cover Sheet; Technical Proposal Cost Information; Summary of Related Activities; Optional form 310, Protection of Human Subjects Assurance Identification/Certification; Government Notice for Handling Proposals?

**A.40. These documents will not count towards the 40 page maximum for the technical proposal.**

41. Which (if any) of the following documents/forms are to be counted toward the 250 page maximum for the business proposal? Proposal Summary and Data Record; Breakdown of Proposed Estimated Cost (plus fee); Offeror's Points of Contact; Disclosure of Lobbying Activities, OMB form LLL?

**A.41. All of these documents will count toward 250 page maximum for the business proposal.**

42. Does HHS expect that clinical assays other than the HI assay (specified in FDA's guidance for pandemic vaccines) will be useful in choosing stockpile product(s)?

**A42. Qualified HAI and microneutralization assays would be expected with appropriate controls and reagents for testing clinical samples for immunogenicity,**

43. Is HHS seeking micro-neutralization assay data?

**A43. See A42.**

44. Can HHS be specific about the expected difference in the level of detail the “regulatory master plan” milestone 1 versus the “regulatory plan” milestone 2?

**A44. The regulatory master plan of milestone 2 should provide more details than the product development plan of Milestone 1.**

45. Under Background, Objectives, the last paragraph (page 6) indicates, “USG support shall not be provided for building a manufacturing facility or purchasing an existing facility.” Is there a potential for subsequent solicitations that may provide USG support for building or purchasing manufacturing facilities?

**A45. There are other solicitations that may provide funding for establishment of manufacturing facilities for pandemic vaccines.**

46. Under Background, Objectives, the last paragraph (page 6) indicates “Activities that may be supported by solicitation include... product- dedicated manufacturing equipment.” Would this also include QA/QC laboratory equipment dedicated to the process?

**A46. No.**

47. Under Milestone III item D. It is noted that “A Production Plan is to contain the “concept” documentation”. To best promote an earliest to market time frame it may be beneficial to accelerate facility documentation. Would HHS consider an alternate to advance this level of documentation to a preliminary or detailed design level?

**A47. See A45.**

48. The solicitation states that “Strategies that can be implemented by influenza vaccine manufacturers worldwide rather than being tied to a specific manufacturer or product would be most advantageous.” (p.5) If an offeror proposes a technique or technology (e.g. a device) to allow for antigen sparing, this seems to imply that locking in with one vaccine manufacturer would be undesirable. Is it, therefore, acceptable for a device company to propose a development program without a collaboration agreement with a specific vaccine manufacturer, but rather with a plan to do clinical testing with several potential vaccine candidates?

**A48. This statement relates to products that may be used with different influenza vaccines. It does prohibit or discourage collaborative arrangements for the product development with a given influenza vaccine.**

49. Can the government provide access to vaccine candidates for such testing?

**A49. No, this is the responsibility of the Offeror to locate potential antigen providers and/or partners.**

50. If the USG cannot provide access to vaccine candidates, are letters from vaccine companies sufficient if they state their intent to provide access?

**A50. Yes.**

51. The solicitation states that "For an antigen sparing strategy to contribute to pandemic preparedness and response that strategy ...must be feasible to implement as in a mass vaccination program." (p.5) What is the definition of "mass vaccination program" in the US context?

**A51. Mass vaccination for a pandemic will entail vaccination of all U.S. citizens in the six month window following the onset of a pandemic and the time frame directly thereafter.**

52. How much consideration will be given to the feasibility of a given strategy for mass vaccination?

**A52. This is part of the technology and methodology approach in the technical evaluation process (section M).**

53. What are the important issues for mass vaccination (e.g. speed of delivery, training requirements, etc)?

**A53. The cited considerations and others including availability of the product.**

54. The solicitation states that one objective is to "Conduct preclinical and clinical testing...to define the type and magnitude of the antigen sparing effect for monovalent influenza vaccine against novel influenza strains (i.e. H5N1 or other subtypes not currently circulating among people) that are considered to have pandemic potential." (p.6) What is the definition of "strains considered to have pandemic potential"?

**A54. For the purposes of this RFP, H5N1 virus strains would have the highest priority.**

55. Would it be acceptable to test the following year's seasonal flu vaccine as a first step, as long as it is currently non-circulating?

**A55. The Offeror may test this vaccine strain, but remember the focus of this RFP is for pandemic viruses.**

56. This program offers development funding with a required commitment by the offeror to make available sufficient product for 150 million doses in 6 months. Is there a commitment by USG to purchase the resulting product?

**A56. See above answer on HHS purchase considerations.**

57. If the manufacturer scales up for manufacturing, is there a possibility that the USG will choose not to purchase the solicited amount of product?

**A57. See A56.**

58. Can the cost of capital investment for manufacturing scale-up be covered by the contract?

**A58. No.**

59. Page 51-52, Section M.3.: Parts of this section are confusing. In particular: Heading 2. Comparative Advantage and Potential Limitations – this heading seems like it belongs with Section 1(c). Sections 2(a), 2(b), 2(c) and 2(d) seem to belong under Heading 1. Methodology and Approach rather than under Heading 2. 2(b) is almost an exact repeat of 1(a). 3(b) asks for facilities capable of producing up to 300 million units over a 6 month period. Elsewhere in the RFP, the production requirement is 150 million units in 6 months. (e.g. page 7 Milestone 3C; page 50 Section M.2. #1b)

**A59. 150 million doses in 6 months is the correct value.**

60. Can we test parallel formulations in the preclinical phase such as two different adjuvants and then make a decision to go forth with only one vaccine to full development?

**A60. Yes, remember an IND submission is due within six months of contract award.**

61. Can we add or subtract consultants, collaborators and investigators after the RFP is filed and during the project if funded?

**A61. The technical panel will evaluate the proposal that is presented before not what may be changed in the future. If circumstances occur where changes have to be made, the contract modifications may be made. However, the proposal provides the cost ceilings.**

62. Could you provide a more complete definition concerning “product-dedicated manufacturing equipment?”

**A62. These are equipment that are used in the synthetic manufacturing of the product (e.g. ultrafiltration skid) but not equipment for general usage in any facility (e.g. microscope).**

63. Will there be coordinated efforts with the required regulatory agencies to facilitate a timely completion of the obligatory milestones.

**A63. The FDA will provide regulatory guidance and review for products emanating from contracts awarded from this solicitation in accordance with federal Statutes and agency policies. See FDA website – A15.**

64. Does the Offeror have to provide storage facilities for the full 150 million doses or can shipments be scheduled as product is released.

**A64. The RFP does provide facility funding.**

65. Can an off-shore facility be used to make batches for clinical trials?

**A65. Yes.**

66. Please clarify: Is it 150 million "doses" or "patients?"

**A66. Doses.**

67. The RFP consistently refers to 150 million doses throughout, except on page 52, where there is a reference to 300 million. What is the significance of this, or is this an assumption of a possible multi-dosing?

**A67. See A59.**

68. What are the circumstances, if any, under which these facilities and equipment could be used to make similar influenza vaccines?

**A68. There are no restrictions from this RFP on facility and equipment usage, but the product must be available in the event of a pandemic.**

69. Is it your expectation that the facility availability would coincide with licensure? What are the ramifications in this regard under fast-track approval?

**A69. Yes. Ramifications are Offeror-specific, as Offerors may be at different stages of product development.**

70. On page 57 of the RFP, under M.7 Animal Welfare, it is stated that "Offerors must submit a plan on how they will comply with all requirements concerning the use of animals for experimentation and be in accordance with any requirements specified and be in accordance of any requirements of the Office of Laboratory Animal Welfare." Please confirm if we are required to include an Animal Welfare section in our proposal if the only proposed animal work is limited to routine release tests performed by a subcontractor.

**A70. If any animal work is performed, then an animal welfare plan must be submitted by Statue.**

71. We already have established and validated aseptic manufacturing facilities in the U.K. for our adjuvant. Would it still be possible to perform the pre-clinical and clinical phases of the proposed work with product made in the U.K., as long as we commit to transferring the manufacture to a US facility post-licensure?

**A71. The clinical lots may be made abroad and used in U.S. clinical studies.**

72. Will the contract support preclinical work as a prelude to clinical work?

**A72. Pre-clinical studies such as toxicology testing will be considered.**

73. The solicitation lists the proposal intent date of 31 March, which we have clearly missed. Does this create a problem? Do we still need to submit a notice of intent to you?

**A73. A proposal may be submitted without a letter of intent being submitted.**

74. Will it be possible for a firm to receive a contract for adjuvant development in regards to dose sparing if their pandemic vaccine production is offshore?

**A74. Yes.**

\* If the adjuvant development and production also is offshore

**A74. Yes, provided the product can be stockpiled in sufficient amounts and time prior to a pandemic.**

\* If the adjuvant development and production is in the U.S.?

**A74. Yes.**

75. Will it be possible for a firm to receive a contract for adjuvant development in regards to dose sparing with no pandemic vaccine capacity?

**A75. Yes, provided that the data support the product as a stand alone product that may be used with an influenza vaccine.**

\* If adjuvant is developed and produced offshore?

**A75. Yes.**

\* If adjuvant is produced domestically?

**A75. Yes.**

76. Will it be possible for a firm to receive a contract under this solicitation for adjuvant development in combination with a trivalent non-pandemic influenza vaccine to demonstrate the adjuvant's ability to increase trivalent vaccine efficacy?

**A76. The focus of this solicitation is on pandemic vaccines. Development of an adjuvant for seasonal influenza vaccine is not the main intent. Comparability and efficacy studies in the appropriate populations to show an adjuvant effect on seasonal influenza vaccine as compared to the immunogenicity of a pandemic influenza vaccine with and without the adjuvant may be considered as an adjunct to the proposal .**

77. Would an aerosol delivery device that has 5x to 10x increased efficiency (thereby stretching vaccine supplies 5 to 10 times further) by providing both high efficiency aerosolization and highly respirable particles for pulmonary delivery of an unspecified vaccine be considered for funding?

**A77. Yes.**

**Questions and Responses edited from the transcript of the Pre-Proposal Conference held April 18, 2006 in Washington, D.C. at the Department of Health and Human Services;**

78. Will the awardee be expected to use the same H5N1 virus for testing? Will HHS stipulate or provide a specific virus to be used?

**A78. First of all, for the virus reference antigen that's needed for potency testing, we have an arrangement with the FDA that there has been a virus reference antigen because it has been made by a validated process. That will be available. You need to contact Jerry Weir at the FDA, and they will be able to ship not only the virus reference antigen for H5N1 that was prepared against the Vietnam 2003 1203 isolate, but also the sheep antiserum that is a companion antiserum for doing the SRDS. That's the first thing. As -- second is as we find a need to have other H5N1**

**virus vaccine candidates developed such as a clade 2 isolate, similar virus reference antigen lots and antiserum will become available also. That's something the Department has been doing and will continue to do so in the future so that the manufacturers will have a common set of reagents there and that you don't have to spend your time with that because these have been already developed and already calibrated with other manufactured products. Where are we right now? Well, certainly the -- what we would recommend is the 1203 strain and that's equal to the NIBRG 14 from NIBSC for the Vietnam -- for Vietnam isolate from 2004 primarily on the merits of its production ability. For the clade 2, there are three isolates that are available or will become available. The H5N1 Indonesian 0505 from CDC from Nancy Cox's lab has been granted -- has been instructed, tested, shown to be apathogenic and noninfectious for birds in man and ferrets also and that the USDA has granted select agent exemption to that. So that virus reference antigen is available -- virus reference strain is available. There are two virus reference strains that St. Jude is working on to make you aware of that for clade 2. There's one from China and one from Mongolia. One of them is much further ahead than the other, and I suggest you contact Dr. Rob Webster about that. There -- John Wood's lab in the UK at NIBSC has one that is for the Turkey isolates of the clade 2 H5N1 viruses. However, they are further behind right now, and so those won't be available for some time. So, we're basically -- if you look at WHO, we're -- these are similar guidance that they would give you also. So, what we would do is have you contact the WHO virus reference lab. Any of those three would be more than happy. I do point out though that the USDA has gotten more stringent on their requirements and it would be a good idea to talk to them about importation of these virus reference strains and other materials from highly pathogenic avian influenza viruses.**

79. Do the protection of human subject form and technical proposal cost information form count against the 40-page limit for the technical proposal? Good question.

**A79. No, they do not.**

80. When a company chooses to pass on this procurement, will it be eligible to put on a future procurement contract?

**A80. The answer is -- it's up to the potential offeror. I mean we have -- we have no exclusions. It's whoever's on the dotted line at the end when the proposal is put -- is submitted is who we're going to review. So, if you're on several proposals, then I would suggest that you do put that in there and then how you -- how you will choose if you are given -- if the contractors were given more than -- if you're on more than one award how you would choose to down select yourself. So, which should be an easy -- a decision we'd all like to have.**

81. Since this is a cost-reimbursable contract, will the IP be given out in stockpile contract?

**A81. The answer's no. No, I mean your IP is your IP. If IP is developed with government funds, then the government has then the ability to use that technology if it's -- if it needs to in -- in government contracts for emergency or such, but we're not going to go and give your information over to somebody else a priority.**

82. Clarification, the time for those of you that are -- are like I am, and you need to know exactly the last minute you can submit your proposal, it is?

**A83. 3:00 p.m. (EST) May 2, 2006**

83. Is there an expectation that contracts to RFP 05-04 will be awarded prior to the submission date of this RFP?

**A83. It could happen. I think that's probably all we can say at this point.**

84. Does the Department anticipate additional funding will be available under RFP 05-04 for phase III clinical trials in licensure of pandemic vaccine?

**A84. Well, this is not germane to this, but I will answer it, and that is that not only this, but other efforts under 05-04 and other projects and -- and other programs within our overall scope will hopefully receive funding in FY '07 and FY '08 as part of the President's initiative that he set out last November. So, we would hope that all of those things are funded in the coming year.**

85. Will you place the names and companies of attendees on your website?

**A85. No, we're not going to. No, not for this particular conference. Worth mentioning, on FedBizOpps there's an interested vendors list, IVL, so, if you want basically the world to see that you're interested in proposing on this particular program, you can register as an interested vendor, and they can then find out that way, but we're 're not going to name attendants.**

86. When will budget templates be available?

**A86. The templates are going to also be posted with the amendment when we send out the responses to the questions.**

87. And two more questions regarding the statement that offerers are responsible for procurement of antigen. Is that true also for antigen-sparing devices that operate independently of the vaccine manufacturing process?

**A87. Yes. Offerors will be responsible for that.**

88. Which items are not included in the page count in the technical proposal? Certainly the cost proposal wouldn't count against it.

**A88. Any information that's not pertinent to the statement of work, please put in 250 pages, allows for the technical appendices, and that should be enough room in the appendices for -- for those peripheral documents.**

END