

Statement of Work

Independently and not as an agent of the Government, the Contractor shall furnish all services, qualified personnel, material, equipment, and facilities, not otherwise provided by the Government, as needed to perform the Statement of Work below:

Definitions

HIV	Human immunodeficiency virus
SIV	Simian immunodeficiency virus
BSL2/BSL3	Biosafety level 2/Biosafety level 3
PBMC	Peripheral blood mononuclear cells
SHIV	Chimeric simian/human immunodeficiency virus
Ad5	Adenovirus type 5
DNA	Deoxyribonucleic acid
mRNA	Messenger ribonucleic acid
PCR	Polymerase chain reaction
RNAs	Ribonucleic Acids
HTLV	Human T cell leukemia/lymphoma virus
ELISA	Enzyme linked immunosorbent assay
TCID ₅₀	50% tissue culture infectious dose
MHC	Major histocompatibility complex
TRIM5	Tripartite motif-containing Motif 5

The contractor shall provide ongoing research support activities in areas including cell culture and virology, immunology, protein biochemistry, molecular biology, storage of biological material and delivery of specimens for the Vaccine Branch, Center for Cancer Research, of the National Cancer Institute, Bethesda, Maryland. In performance of this work, the Contractor shall conduct the following:

I. Transition In

The successor Contractor shall ensure a smooth transition between the incumbent and the new award, if required:

- a) Cooperate with the former Contractor to ensure there is no break in continuity of research support. The transition shall be fully implemented before the completion date of the former contract (by October 31, 2014). The successor Contractor shall have full operational capacity at the time of award.
- b) Implement an orderly, secure, and efficient transition of all activities, materials, data, and other documents from the former contractor to the successor Contractor or the Government.
- c) Use an appropriately bonded moving agent, experienced in secure transfer of biological materials under appropriate storage temperatures, to safely move all materials

maintained under the current contract to the successor Contractor or the Government, without any interruption of research services.

d) Ensure that adequate computer service and data storage is available for receiving and maintaining data records.

e) Ensure that adequate equipment is in place for receipt and storage of biologic samples at appropriate temperatures.

II. Core work

A. Pickup and delivery of Biological specimens

The Contractor shall arrange for pick-up and delivery of specimens, Monday through Friday, except Government holidays, between the Contractor's site and laboratories on the NIH campus (9000 Rockville Pike, Bethesda, MD 20892-1360), or NCI Fort Detrick campus (810 Schreider Street #1, Frederick, MD 21702). Pick-up/delivery times shall be specified by the COR or other NCI Investigators and will be approximately between 8:00 AM and 4:30 PM local time. The Contractor shall also arrange shipment of specimens or reagents to outside investigators as requested by the COR. The Contractor shall package biological specimens according to U.S. Department of Transportation regulations.

B. Immunological assays and reagent preparation

1. Assess the serologic status of human or animal samples supplied by NIH and evaluate the prevalence of virus present within the host population. Serum or plasma samples shall be tested for the presence of antibodies to human and other mammalian viral proteins or peptides (HIV, SIV, HTLV-1/2) using such techniques as ELISA, Western blot, and antigen capture assays. Pepscan assays shall be conducted to determine specific antibody epitopes recognized and ELISAs shall be conducted to determine antibody isotypes. The Contractor shall, upon completion of assays, document the results achieved and report data in sufficient detail in accordance with SECTION F.2. DELIVERIES (see a.1. Data Reports).
2. Provide purifications of lymphocytes from blood, lymph nodes or other tissues from animals or humans and provide fresh and viable cells to the Contracting Officer Representative (COR) or other NCI Investigator. The Contractor shall deliver fresh viable cells in accordance with SECTION F.2. DELIVERIES (see b.2. Biological Specimens Delivery) unless otherwise requested by the COR.
3. Provide purified, biochemically characterized and biologically active (where appropriate) native viral proteins from infected cells or conditioned media and from bacterial or mammalian expression systems. Provide His-tagged HIV or SIV gp120. Recombinant vectors expressing the proteins or peptides shall be supplied by NIH and could include regulatory, enzymatic and structural proteins. Purified proteins shall meet a

predetermined level of purity specified by the COR. The Contractor shall also furnish data to the COR confirming that the proteins are of the quantity and meet the specifications of purity and biological activity agreed to between the COR and the Contractor before work was started on the product. In performance of this task the Contractor shall have the capability to provide:

- i. between 10 and 30 mg of both SIV_{mac251} and HIV native gp120,
- ii. between 5 and 15 mg of SIV_{E660} native gp120,
- ii. between 5 and 10 mg of SIV p27,
- iii. between 3 and 7 mg of SIV Nef,
- iv. between 5 and 15 mg of active HIV Tat, and
- v. IgG purified from between 900 and 2700 ml of rhesus macaque plasma, and IgA purified from plasma or mucosal secretions. The purified Igs shall contain low endotoxin levels.
- vi. Provide His-tagged HIV and SIV gp120.

The Contractor shall provide proteins and data in accordance with ARTICLE F.2. DELIVERIES (see b.2. Biological Specimens Delivery).

4. Synthesize and provide between three (3) and six (6) sets of overlapping peptides, representing proteins from the HIV, SIV, or adenovirus genomes. These shall be 15-mers overlapping by 11 amino acids unless otherwise specified by the COR. The produced peptides shall be delivered in accordance with ARTICLE F.2. DELIVERIES (see b.2. Biological Specimens Delivery).
5. Sort antigen specific B-cells and produce and characterize monoclonal antibodies from 1 to 2 cloned B cell lines provided by the government. Antibodies shall be well characterized for titer, for specific recognition of the protein antigen, and for blockage of the biological function of the protein where appropriate. The produced antibodies shall be delivered in accordance with ARTICLE F.2. DELIVERABLES (see b.2. Biological Specimens Delivery).

C. Viral stock preparation and virological assays

1. Provide between one (1) and three (3) purified and titered stocks of attenuated recombinant poxviruses containing with titers of 10^9 to 10^{10} TCID₅₀/ml as requested by the COR. The initial viral inocula shall be provided by the Government. The stocks of recombinant viruses shall be stored until requested by the COR. The Contractor shall deliver viral stocks in accordance with SECTION F.2. DELIVERIES (see b.2. Biological Specimens Delivery) unless otherwise requested by the COR.
2. Provide between two (2) and five (5) titered stocks of aliquots of field isolates for *in vitro* use from virus-infected humans and non-human primates at low passage number on human or non-human primate PBMC. Provide one to two primary isolate stocks of SIV or SHIV strains for use as *in vivo* challenge stocks, of sufficient titer for mucosal as well

as intravenous administration. Provide aliquots of high-titered T-cell-line-adapted (TCLA) stocks of HIV or SIV for *in vitro* use. This work shall be conducted in BSL2/BSL3 laboratories. The viral stocks shall be maintained in liquid nitrogen storage until requested by the COR. The Contractor shall deliver viral stocks in accordance with SECTION F.2. DELIVERIES (see b.2. Biological Specimens Delivery) unless otherwise requested by the COR.

3. Conduct *in vitro* culture and detection of retroviruses samples of peripheral blood and/or tissues, provided by the Government, of humans or non-human primates. When requested, the Contractor shall determine viral infectious units in cells or tissues by end point dilution. Retroviruses shall include HIV, SIV, or SHIV. This work shall be conducted in BSL2/BSL3 laboratories. The Contractor shall receive samples from the Government and/or Government contractors, as requested by the COR. The Contractor shall commence *in vitro* culture and detection within one (1) hour of notification by the COR of a sample being delivered to the Contractor. In the event the Contractor has not received the sample within 50 minutes of the COR's notification of the sample delivery, the Contractor shall immediately notify the COR. The Contractor shall provide the result of culture and detection of retroviruses in accordance with SECTION F.2. DELIVERIES (see a.1. Data Reports).
4. Conduct real time PCR assays for SIV gag in plasma and SIV gag in tissues. Purify and quantitate mRNA in plasma or tissue samples of animals or humans by real time PCR. Quantitate viral RNAs, including HIV and SIV as requested by the COR. The real time PCR for viral RNAs shall be sensitive to 50 copies/ml plasma. The Contractor shall conduct real time PCR assays weekly over 5 to 15 weeks on 30 to 60 plasma samples associated with repeated low-dose SIV or SHIV challenges with a turn-around time of five (5) days. The Contractor shall document in sufficient detail each step taken in performing the tasks delineated in this section and provide data collected in accordance with ARTICLE F.2. DELIVERABLES (see a.1. Data Reports).
5. Conduct assays to quantitate viral DNA levels by real time PCR for SIV from cells of non-human primates. The Contractor shall provide the results of the proviral DNA assays in a report in accordance with ARTICLE F.2. DELIVERABLES (see a.1. Data Reports).

D. General molecular assays and reagent preparation

1. Determine MHC class I haplotypes (1 or more of the following: Mamu A*01, A*02, B*08, B*17), and TRIM5a alleles of rhesus macaques.
2. Design, synthesize, and purify codon-optimized genes encoding cellular or viral proteins for eukaryotic or prokaryotic expression. For the individual genes produced the Contractor shall provide between three (3) and six (6) mg of product. Examples include HIV or SIV primary isolate envelopes (gp160). Deliver the synthesized gene and/or the

purified expressed protein to the COR in accordance with ARTICLE F.2. DELIVERIES (see b.2. Biological Specimens Delivery).

3. Prepare and provide pre-clinical grade plasmid DNA products containing minimal levels of endotoxin and encoding HIV or SIV genes for vaccine studies. The Contractor shall deliver the plasmid DNAs upon completion in accordance with SECTION F.2. DELIVERIES (see b.2. Biological Specimens Delivery) unless otherwise requested by the COR.

E. Storage of biological materials

1. Provide storage for viable cell lines, titered field isolates, viral challenge stocks and viable cell specimens from inoculated and immunized animals as requested by the COR. The Contractor shall maintain a backup system capable of maintaining materials stored at the required temperatures. The storage capacities and temperature requirements are:
 - 1) 25cubic feet of minus 180 degree Celsius storage maintained by liquid nitrogen,
 - 2) 185 cubic feet of minus 80 degrees Celsius storage, and
 - 3) 75 cubic feet of minus 20 degrees Celsius storage.

F. Transition Out

The current Contractor shall:

1. Cooperate with the successor contract to ensure there is no break in continuity of research support. The final transition shall be fully implemented before the completion date of the contract.
2. Plan and coordinate an orderly, secure, and efficient transition of all activities, materials, data, and other documents to the successor Contractor or the Government. A description of transition activities and timelines shall be provided in a Draft and Final Transition Plan, which shall be reviewed and approved by the COR and Contracting Officer.

Draft Transition Out Plan: Six (6) months prior to the completion date of the contract, the Draft Transition Plan shall be submitted for review and comments by the COR and Contracting Officer. Elements to be addressed are:

- a) An inventory of samples, materials, and products to be transferred.
- b) Clear labeling and identification of vials and sample containers to be transferred.
- c) Government-owned property to be transferred and equipment maintenance records.
- d) Materials that will be under production at the end of the contract which shall need to be transferred together with appropriate SOPs for completion of the production.

- e) Electronic files of all data and labeled and inventoried paper files to be transferred.
 - f) Transition activities, timelines, and staff needed to implement the transfer to the successor contractor.
3. Final Transition Out Plan: Four (4) months prior to the completion date of the contract, the Final Transition Plan shall be submitted for review and approval by the COR and the Contracting Officer. The Final Transition Plan shall present a comprehensive logistical analysis for the orderly and safe transition of research support functions to a Successor Contractor. This plan shall include:
- i. The tasks associated with secure transfer by the successor contractor of stored materials, reagents, all related data, and any Government-furnished property.
 - ii. A timeline for the complete, timely and effective transfer of data, and research materials held by any subcontractor(s) to the Successor Contractor, and performance of all necessary transition, transfer and closeout functions on each subcontract.
 - iii. A timeline for delivery to the successor Contractor and/or the Government, the following additional items:
 - a. a computerized inventory of samples, materials, and products being transferred.
 - b. lists of all materials still under production with any relevant SOPs for completing the production
 - c. electronic files of all data
 - d. labeled and inventoried paper files
 - e. listings of all Government-owned property and equipment maintenance records.
 - iv. A plan for maintenance of full operational capacity through the completion date of the contract.

III. Optional work : Determination of CD4, CD8, and B cell counts

- a) Provide CD4/CD8 and B cell counts (percentages and absolute numbers) from 500 to 1500 blood samples per year from non-human primates. The Contractor shall document in sufficient detail each step taken in performing the tasks delineated in this section and provide data collected in accordance with ARTICLE F.2. DELIVERABLES (see a.1. Data Reports).