U.S. Department of Health and Human Services
National Institutes of Health
National Institute of Allergy and Infectious Diseases (NIAID)

RFP-NIH-NIAID-DAIDS-06-15
Simian Vaccine Evaluation Units (SVEU)

1. **OFFERORS ARE RESPONSIBLE FOR ROUTINELY CHECKING THE FOLLOWING WEBSITE FOR ANY SOLICITATION AMENDMENTS. NO ADDITIONAL NOTIFICATION OF ANY AMENDMENTS WILL BE PROVIDED BY THIS OFFICE.** http://www.fedbizopps.gov/

2. **SECTION A – SOLICITATION/CONTRACT FORM -- PURCHASE AUTHORITY: FAR 1.602-1**
NOTE: The issuance of this solicitation does not commit the government to an award.

3. **Issue Date:**	4. **Due Date:** August 10, 2005	5. **Small Bus. Set-Aside:** [ ]Yes [x] No
May 11, 2005	**Time:** 4:00 p.m. EST	**8(a) Set-Aside:** [ ]Yes [x] No
		NAICS #: 541710
		(See Part IV, Section L.)

6. **Just In Time:**	7. **Number of Awards:**	8. **Technical Proposal Page Limits:**
[x] No [ ] Yes (See Part IV, Section L.)	[ ] Only 1 Award [x] Multiple Awards	Number of Copies: See Part III, Section J (Proposal Submission Instructions) Page Limitations: 150 **excluding Appendices**

9. **Issued By:**	10. [x] **NIAID reserves the right to make awards without discussion.**	
Jacqueline C. Holden Contracting Officer Contract Management Program, DEA NIH, NIAID 6700-B Rockledge Drive Room 3214, MSC 7612 Bethesda, MD 20892-7612	11. **Options:** **[x] No** **[ ] Yes** (See Part IV, Section L.)	12. **Period of Performance:** **May 8, 2006 – May 7, 2013**

13. **Primary Point of Contact:**	14. **Secondary Point of Contact:**	15. **Protest Officer:**
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16. **COLLECT CALLS WILL NOT BE ACCEPTED. FACSIMILE SUBMISSIONS ARE NOT ACCEPTABLE.**

17. Offers will be valid for 120 days unless a different period is specified by the Offeror on the form entitled "Proposal Summary and Data Record, NIH-2043" (See Part III, SECTION J – Attachments)

18. **DELIVERY ADDRESS INFORMATION**

19. **Hand Delivery or Overnight Service:**	20. **U.S. Postal Service or an Express Delivery Service**
Michelle Scala Contract Management Program, DEA NIAID, NIH 6700-B Rockledge Drive, Room 3214 Bethesda, MD 20817	Michelle Scala Contract Management Program, DEA NIAID, NIH 6700-B Rockledge Drive, Room 3214, MSC 7612 Bethesda, MD 20892-7612

21. The **Official Point of Receipt** for the purpose of determining timely delivery is the address provided in Block 19, above. The original paper copy with original signatures is the official copy for recording timely receipt. If the original paper copy of your proposal is not received by the Contracting Officer or Designee at the place and time specified, then it will be considered late and handled in accordance with HHSAR 352.215-70 entitled "Late Proposals and Revisions" located in this Solicitation. FACSIMILE SUBMISSION OF PROPOSALS IS NOT ACCEPTABLE.

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SIMIAN VACCINE EVALUATION UNITS (SVEUs)

BACKGROUND

The mission of the Division of AIDS (DAIDS) of the National Institute of Allergy and Infectious Diseases (NIAID) is to help ensure an end to the HIV/AIDS epidemic by increasing basic knowledge of the pathogenesis and transmission of the human immunodeficiency virus (HIV), supporting the development of therapies for HIV infection and its complications, and supporting the development of vaccines and other prevention strategies. This mission is carried out by three Programs: the Basic Sciences Program (BSP), the Therapeutics Research Program (TRP), and the Vaccine and Prevention Research Program (VPRP).

The VPRP, DAIDS, supports Simian Vaccine Evaluation Unit (SVEU) contracts to conduct preclinical evaluations of the immunogenicity and efficacy of promising simian immunodeficiency virus (SIV) and HIV candidate vaccines in nonhuman primates. Studies are conducted at the initiation of NIAID, and vaccines to be evaluated are selected by NIAID. The SVEU program was initiated in 1991 with the award of three contracts, was renewed and expanded in 1996 to five awards, and was renewed again in 2001 with the award of the current three contracts. The current SVEU contractors are (1) the University of Washington Regional Primate Research Center: N01AI15431, (2) Advanced BioScience Laboratories: N01AI15430, and (3) Southern Research Institute: N01AI15429. These contracts expire in April, 2006. The purpose of this solicitation is to recompete this research program and award multiple new contracts for a term of seven years.

The SVEU contracts provide the nonhuman primates and the scientific and technical expertise necessary to conduct preliminary studies of new vaccines; conduct larger-scale studies of vaccines that have already demonstrated promise; evaluate the immunogenicity and safety of candidate HIV vaccines (or immunogenicity, safety, and efficacy of SIV vaccines which parallel HIV vaccines in approach) in anticipation of Phase I human clinical trials; and conduct comparative studies on vaccines and/or adjuvants from multiple sources. The SVEUs may also conduct studies with passively administered vaccines and *in vivo* titrations of virus challenge stocks when requested. In addition to providing nonhuman primates for the studies, the SVEUs are expected to immunize animals with candidate vaccines; conduct initial assessments of immune responses; challenge the non-human primates with infectious virus; and determine whether or not the animals become infected.

SVEUs may also conduct microbicide studies in order to evaluate the ability of topically administered microbicides and other antiviral substances to block infection of non-human primates with virus administered vaginally or by other mucosal routes. In addition, in order to maximize the use of resources, animals that have become infected with viruses after a vaccine study, virus titration, or microbicide study may be used for pilot studies with antiviral agents administered alone or in conjunction with a vaccine.

The SVEU contracts are an important component of NIAID's program for the preclinical evaluation of vaccines. The SVEUs complement NIAID-supported basic research studies and vaccine evaluation studies being funded through investigator-initiated research grants. The SVEUs are used to evaluate the immunogenicity and efficacy of vaccines developed by investigators under R01 (investigator-initiated research) grants, HIVRAD (HIV Vaccine Research and Design Program) grants, and IPCAVD (Integrated Preclinical-Clinical AIDS Vaccine Development) grants, as well as vaccines provided by companies or other researchers. SVEU contracts conduct studies at the initiation of the NIAID. SVEU investigators may not initiate or conduct studies on the contract without NIAID pre-approval.

Additional information relevant to this solicitation is provided in the following Appendices:

Appendix A – Primate Immunology and Virology Support Contracts:
A description of the current DAIDS support contracts for primate immunology and virology laboratory services.

Appendix B - Sample of AIDS Vaccine Study Protocol Data Input for DAIDS SVEU Database
Sample screens from the DAIDS SVEU Database.

Appendix C – Examples of Publications Resulting from AIDS Vaccine Studies Conducted by the SVEUs

STATEMENT OF WORK

Scope:

The scope and intent of the contracts for the Simian Vaccine Evaluation Units (SVEUs) is to enable the NIAID to use nonhuman primates to conduct studies that advance the development of effective AIDS vaccines, and to a less extent, the development of effective microbicides and other prevention modalities, and immune therapy. The SVEUs will use state-of-the-art techniques and technologies in evaluating promising AIDS prevention strategies in nonhuman primate models and will incorporate new and improved techniques and technologies into the studies conducted throughout the contract period.

The major functions to be carried out by the Simian Vaccine Evaluation Units (SVEUs) are as follows:

1. Initial Transition
2. Acquisition and testing of non-human primates
3. Housing and care of non-human primates; maintenance of animal records
4. Protocol Development
5. Conduct of Studies
6. *In Vitro* Laboratory Immunologic and Virologic Assays
7. Storage and shipment of materials
8. Entry of SVEU study protocols, information, and data into the DAIDS SVEU database
9. Communications with the Project Officer
10. Final Transition

Independently, and not as an agent of the Government, the Contractor shall furnish all services, qualified personnel, materials, equipment, animals, and facilities, not otherwise provided by the Government under the terms of this contract, as needed to perform the work set forth below.

1. Initial Transition

At the initiation of the contract, provide a plan and timetable for having the proposed facility ready to start conducting studies. If it is necessary to assume the activities of a current SVEU contractor, coordinate with the incumbent contractor(s) those activities required to achieve an orderly initial transition of contract resources, including disposition/movement of nonhuman primates, study specimens and data, and Government-owned equipment. The transition must be accomplished within the first 45 calendar days following the effective date of the contract. The Final Transition Plan of the incumbent contractor(s) will be provided by the NIAID Project Officer and will specify the approved transition requirements, as well as the methods and time frame for implementing the transition.

Within two (2) weeks after contract award, the Contractor shall submit a contract specific information security plan for review and approval by the NIAID.

2. Acquisition and testing of Nonhuman Primates

a. In the first year of the contract, acquire from approximately 100 to approximately 300 nonhuman primates for studies to be conducted under this contract. The nonhuman primates may be obtained either from breeding colonies at the Contractor's facility or from outside sources. In the second and subsequent years of the contract, acquire approximately 50-150 additional nonhuman primates per year. These animals may be moved into the SVEU facility, as needed to maintain the full complement of animals, or may be held off-site until ready to be used for studies. Primary emphasis will be on rhesus macaques (Macaca mulatta) of Indian origin. However, because of the continuing shortage of these animals, SVEUs may be requested to house and conduct studies utilizing Chinese-origin macaques, or other nonhuman primate species, such as pig-tail macaques (Macaca nemestrina), cynomolgus monkeys (Macaca fascicularis), African green monkeys (Cercocebus atys), or baboons. Housing for studies with baboons is not required to be at the SVEU facility, and may be provided off-site by a subcontractor. The decision of which nonhuman primate species to be used for a study will be made jointly by the NIAID Project Officer, the vaccine provider, and the SVEU Principal Investigator, with the NIAID Project Officer having the final approval authority.

b. Provide tuberculosis (TB)-free nonhuman primates that are also free of infection with simian immunodeficiency virus (SIV), simian T-cell lymphotrophic virus (STLV), and simian type D retrovirus (SRV). To confirm that

animals are free from infection with these retroviruses, conduct testing of the nonhuman primates to screen for these viruses prior to purchase and shipment to the SVEU facility. In addition, test the nonhuman primates for the presence of antibodies to simian herpes B virus so that their serostatus is known.

c. Quarantine the nonhuman primates as they arrive at the SVEU facility. While in quarantine, conduct sequential tuberculosis (TB) testing to confirm TB-free status, and repeat retroviral testing to confirm virus-free status.

3. Housing and Care of Nonhuman Primates; Maintenance of Animal Records

a. Provide well equipped and maintained, AAALAC (Association for the Assessment and Accreditation of Laboratory Animal Care)-accredited facilities for nonhuman primates and house from approximately 100 to approximately 300 nonhuman primates in appropriate biohazard containment facilities, using appropriate biosafety procedures to care for and handle virus-infected animals. Animals may be housed in BSL-2 biohazard containment facilities until exposure to infectious SIV, SHIV or related retrovirus. After exposure, biohazard containment shall be at the Biosafety Level-2 (BSL-2) using BSL-3 practices.

b. Comply with the Public Health Service Policy on Humane Care and Use of Laboratory Animals. This policy may be accessed at http://grants1.nih.gov/grants/olaw/references/phspol.htm.

c. Provide care, routine health surveillance, and environmental enrichment for the nonhuman primates, and provide and conduct clinical laboratory testing (such as complete blood counts, parasite evaluations, bacterial culture, and serum chemistry testing) for the animals. Provide CD4 and CD8 T cell determinations and total lymphocyte counts of blood samples as required by study protocols. Record and maintain clinical observations and clinical laboratory data results for each animal. The veterinary and animal care staff shall perform and record observations, including each animal's health status, any treatments received, and the results of periodic weighing. The NIAID Project Officer shall be notified if an animal is sufficiently ill for the veterinarian to recommend euthanization.

d. Perform and document tuberculosis (TB) testing of all animals maintained under this contract on a quarterly basis in order to maintain a TB-free facility. Animals that test positive for TB shall be euthanized as soon as possible, with timely notification of the NIAID Project Officer.

e. Provide for (on-call) veterinary coverage of the animal facility 24 hours a day, seven days a week, provide at least daily observation of the health status of each animal, including weekends and holidays.

f. Provide standard technical and veterinary assistance, as needed, for the performance of routine procedures, such as inoculation and bleeding of the nonhuman primates. Provide veterinary capability for the performance of all surgical procedures, such as vaginal or rectal pinch biopsies, lymph node biopsies, and post-mortem examinations.

g. Provide and manage a security system to prevent unauthorized entry into the animal care facility.

h. At the termination of a study, the end of the contract, or when requested by the NIAID Project Officer: (1) move the animals onto another study at the SVEU, which may include a pilot study of the efficacy of antiviral agents, or a vaccine study in the presence of antiviral agents; (2) euthanize animals according to humane procedures approved by the Contractor's Institutional Animal Care and Use Committee (IACUC); or (3) ship the animals (including virus-infected animals) to another SVEU or another animal facility. Shipment of any SIV-infected animals shall be conducted using appropriate biocontainment practices and shall conform to applicable regulations for intra-state or interstate transport,

i. Support per diem costs and associated care-related costs for off-site housing of nonhuman primates, in addition to the approximately 100-300 nonhuman primates to be housed at the SVEU facility as described in items 3a-h above, when agreed upon by the NIAID Project Officer and the SVEU Principal Investigator. This may include charges paid to a nonhuman primate breeding colony to maintain a breeding group of nonhuman primates intended solely for use by the SVEU; per diem charges paid to a nonhuman primate facility to house nonhuman primates that have been purchased by the SVEU but are too young to use for studies at the SVEU; and per diem costs for animals that have been purchased from breeding facilities or other sources and need to be housed temporarily until space becomes available to move them into the SVEU facility.

4. Protocol Development

a. Develop a protocol for each approved study. Protocols are to be developed in conjunction with the NIAID Project Officer, other appropriate NIAID staff, and other collaborators participating in the study, especially those providing vaccines, microbicides, etc., for the study and those conducting immunological or virological assays for the study.

Protocols shall include:

(1) contact information for the researcher providing the vaccine(s), microbicides, etc., and for the SVEU investigators and others involved in the study;

(2) background information and description of the vaccine(s), microbicides, etc., being evaluated;

(3) a description of the challenge virus;

(4) the macaque species being used and the number of animals required for the study;

(5) a study chart outlining the number of animals per group, vaccine(s), microbicides, etc. each group will receive, the times of immunizations or administrations and the proposed time(s) of viral challenge;

(6) a listing of the assays to be conducted during the study, including which laboratories will conduct the assays;

(7) dated schedules of immunizations/administrations, blood and tissue specimen collection, and viral challenge; and

(8) other information about the animals, the vaccine or adjuvant, the assays, or the protocol that may be requested by the NIAID Project Officer or other participants in the study.

b. Obtain final written approval of each study protocol from the NIAID Project Officer before initiation of the study.

c. Submit protocols to the Contractor's IACUC for approval.

d. Amend the protocols during the course of the studies, as necessary, after concurrence of the NIAID Project Officer.

5. Conduct of Studies

SVEUs are to conduct studies at the initiation of the NIAID Project Officer. SVEU investigators shall not initiate or conduct studies on the contract without NIAID pre-approval.

According to approved protocols, conduct:

- Vaccine studies
- *In vivo* titrations of virus stocks
- Route of immunization or route of infection studies and other preliminary studies as may be required to carry out a vaccine study
- Evaluations of the efficacy of passively administered antibodies, microbicides, and other anti-viral substances; and other preliminary studies as may be required to carry out these studies
- Generation of virus stocks
- Pilot antiviral drug studies and/or immunotherapy studies with animals after they have become infected in other SVEU studies

a. When requested by the NIAID Project Officer, determine and record the Major Histocompatibility Complex (MHC) type of the nonhuman primates to be involved in a study, or ship specimens to a laboratory approved by the NIAID Project Officer for such analysis.

b. Immunize/treat animals with candidate vaccines, adjuvants, antibodies, microbicides or other anti-viral substances, using the doses, schedules, and routes indicated in the approved protocols. Inoculation routes shall include one or more of the following: intramuscular, intradermal, subcutaneous, intranasal, intravaginal, intrarectal, intravenous, oral, or other routes designated by the approved protocol. Candidate vaccines, adjuvants, microbicides, and other materials, will be provided by or through NIAID.

c. Draw blood or obtain other fluids or tissue samples prior to immunization/treatment and from immunized/treated animals at times and of volumes/quantities specified in the approved protocols for immunological assessment and other tests and assays, as indicated in the approved protocols. Specimens to be collected may include: sera, mucosal (nasal, vaginal and rectal) secretions/washes, lymphocytes, cerebrospinal fluid, fecal samples, broncho-alveolar lavages, biopsies of lymph nodes and mucosal tissues, or others as designated by the approved study protocol. Samples shall be processed as specified in the protocols and, as specified in the approved protocol, either assayed at the SVEU, frozen for storage at the SVEU, sent to the NIAID contract Primate Immunology Laboratories currently located at Harvard University and Duke University, or sent to another appropriate laboratory.

d. Monitor immunized/treated animals for toxicity, and monitor both immunized/treated and virus-challenged animals for general health status (i.e., weight, standard blood and chemistry profiles, opportunistic infections, and other assessments specified in the approved protocol). Maintain records of this clinical information.

e. With final authorization by the NIAID Project Officer and using appropriate biohazard precautions, challenge immunized/treated and/or control/naive animals with a specific dilution of a titered stock of virus (SIV, SHIV, HIV-2, or related virus) using doses and routes specified in the approved protocols. Routes of administration of the challenge virus shall include one of the following: intravenous, intravaginal, intrarectal, or other route specified in the approved protocol. Virus stocks will be provided by or through NIAID.

f. Using appropriate biohazard precautions, draw blood or obtain other fluids or tissues from the challenged animals for detection of plasma virus RNA, virus isolation by co-culture, detection of virus in tissues or other virological assessment, immunological assessment, and other tests or assays as specified in the approved protocol. Samples shall be processed as specified in the protocols and either assayed at the SVEU, frozen for storage at the SVEU, sent to the NIAID contract Primate Immunology Laboratories, currently located at Harvard University and Duke University, or to the Virology Laboratory, currently located at Advanced BioScience Laboratories, or sent to another appropriate laboratory. Conduct biopsies or necropsies as requested by the NIAID Project Officer.

g. Prepare and utilize standard operating procedures (SOPs) for the tasks delineated in sections a. through f. above, including immunization, blood draws, specimen processing, specimen freezing, specimen storage, specimen shipping, biosafety procedures for handling challenge virus and virus challenges of animals, clinical monitoring, biopsies, necropsy, etc. Submit SOPs for NIAID Project Officer review and approval at the time of contract award. Additional, subsequent SOPs and modifications to current SOPs are to be submitted for NIAID Project Officer review and approval. Share SOPs with other SVEUs or other researchers at the request of the NIAID Project Officer for purposes of ensuring comparability of procedures among the SVEUs. As requested by the NIAID Project Officer, alter or adapt SOPs to achieve comparability of procedures and results among the different SVEUs and with other researchers in the AIDS vaccine field.

h. Provide data and information from the studies to the NIAID Project Officer when requested, and, at the request of the NIAID Project Officer, provide experimental results to the investigators collaborating in the studies and/or to the NIAID Project Officer in a format to be specified by the NIAID Project Officer. **(Refer to section 8: "Entry of SVEU study protocols, information, and data into the DAIDS SVEU Database.")**

6. *In Vitro* Laboratory Immunologic and Virologic Assays

All analyses of material obtained after virus challenge shall be performed in a BSL-2 or BSL2/BSL3 biohazard containment laboratory by trained personnel.

a. Assess the immunological responses of immunized animals and of challenged/infected animals.

Perform immunologic analyses of specimens from animals, as specified in study protocols, before and/or after challenge with SIV, SHIV, or HIV. Specifically: Detect and/or titer antibodies to SIV, HIV, or SHIV, to specific SIV and/or HIV antigens, or to other antigens as specified in the approved protocol. The SVEUs may also conduct other assays of immunological response when specified in the approved protocol, although the majority of other immunological assays will be conducted by the Immunology and Virology Laboratory contractors. For all assays, include appropriate controls, demonstrate the sensitivity and specificity of the assays, and provide quality control of assays. Conduct studies to compare assays with other SVEUs and with the NIAID Primate Immunology Laboratory as requested by the NIAID Project Officer.

b. Assess the virological status of challenged animals to confirm protection from viral challenge or viral infection.

When specified in the study protocol, perform virologic analyses of specimens from animals before (baseline) and at multiple times after challenge with SIV, SHIV, or HIV. Virologic assays may include, for example, the detection or isolation of virus by *in vitro* co-culture of nonhuman primate peripheral blood cells with appropriate naïve target cells; assays for detection of viral RNA or DNA in tissues from the animals; and assays for the detection and quantitation of RNA in plasma from the animals. Include appropriate controls, demonstrate the sensitivity and specificity of the assays, and provide quality control of assays. Conduct studies to compare virologic assays with other SVEUs and with the NIAID Primate Virology Laboratory as requested by the NIAID Project Officer.

c. Conduct *in vitro* titrations of virus challenge stocks.

Using appropriate target cells, determine the *in vitro* titer of virus stocks selected by the NIAID Project Officer.

d. Prepare and utilize SOPs for the immunological and virological assay procedures described in sections a. and b. above, including SOPs for handling and processing material from virus-infected animals. Submit SOPs for NIAID Project Officer review and approval at the time of contract award. Additional, subsequent SOPs and modifications to current SOPs are to be submitted for NIAID Project Officer review and approval. Share SOPs with other SVEUs or other researchers at the request of the NIAID Project Officer. Harmonize, alter or adapt SOPs at the request of the NIAID Project Officer to ensure comparability of results among the different SVEUs and with other researchers in the AIDS vaccine field.

7. Storage and Shipment of Materials

a. Store and maintain an inventory of titered virus stocks and candidate vaccines supplied by the NIAID Project Officer. Store and maintain an inventory of animal specimens collected during the course of the studies conducted under this contract. Provide for appropriate storage at -20°C and -80°C, with monitoring of storage conditions by automatic temperature alarm to guarantee continuous proper storage of virus stocks, candidate vaccines, specimens, and other material.

b. Ship specimens (for example: blood, serum, plasma, cells, tissues, mucosal washes) to the DAIDS Primate Immunology and Virology contractors, and ship specimens to other collaborating investigators as designated in the approved protocol or designated by the NIAID Project Officer, using shipping conditions appropriate for preserving the specimens.

c. For shipment of all specimens, especially shipments of sera, cells, blood and other tissues from SIV-, SHIV-, or other virus-infected monkeys, use biocontainment shipping procedures and containers which comply with International Air Transport Association (IATA) Dangerous Goods Regulations for shipment by air transportation, or with Department of Transportation (DOT) regulations for shipment by ground transportation.

d. At the conclusion of the contract, frozen specimens shall be disposed of in an appropriately biocontained manner or transferred to another contract by the Contractor, as specified by the NIAID Project Officer.

8. Entry of SVEU Study Protocols, Information, and Data into the DAIDS SVEU Database

(The DAIDS SVEU Database is an Oracle-based database, maintained by a separate NIAID contractor and accessed by the

internet via a website that is password protected. The Database shall be used, in addition to any other reporting requirements, to provide a means of monitoring the progress of each study and to centralize data collection for all of the studies conducted under this contract.)

a. Provide the following computer and internet capability to make it possible to access the DAIDS SVEU Database:

1) a computer system (Mac. Windows, Unix, Linux) with:

2) a web browser such as Internet Explorer

3) Microsoft Excel (to view spreadsheet graphs or submit assay data)

4) Access to the Web (via a corporate network or Internet Service Provider (ISP) like Comcast, AOL, NetZero, or Netscape)

5) Availability of IT support on an as-needed basis to resolve any problems with access to the DAIDS SVEU Database web site.

b. Enter SVEU vaccine study protocols and study data into the DAIDS SVEU Database:

1) Enter animal information (for example: animal species, incoming animal number, DOB/age, weight, source/origin, results of tests for TB and viral infections, etc.) into the DAIDS SVEU Database at the time the animals are brought into the SVEU.

2) Enter final approved protocols into the DAIDS SVEU Database.

3) Enter updated information into the DAIDS SVEU Database on the progress of protocols as each immunization, sample collection, and virus challenge is performed.

4) Enter selected clinical data on the animals into the DAIDS SVEU Database, as specified by the approved study protocol. The animal clinical data may either be entered into the DAIDS SVEU Database manually, or if the SVEU has an internal clinical database, the NIAID contractor managing the DAIDS SVEU Database will work with the SVEU to establish a direct link with the SVEU clinical database for the purpose of transferring the data.

5) Enter immunological and virological data into the DAIDS SVEU Database from assays performed for a SVEU study at the SVEU site.

6) Establish an on-site quality assurance/quality control system to ensure accuracy of all entered data as well as the timely resolution of inconsistencies including those identified by the DAIDS SVEU Database contractor.

9. Communications with the NIAID Project Officer

a. Establish electronic communications with the NIAID Project Officer sufficient to support exchange of e-mail and the submission of data files and reports when requested.

b. Provide, via telephone or e-mail, periodic updates of project status when requested by the NIAID Project Officer.

c. Submit project plans, project reports, and annual reports in a timely fashion and in accordance with the Reporting Requirements and Deliverables section of this RFP.

d. Plan and conduct annual site visits, including presentation of data from and the status of on-going projects, for NIAID Program and Contract Staff.

e. Meet with the NIAID Project Officer at least once a year at a meeting in Bethesda, MD or at a scientific meeting to be designated.

10. Final Transition

If, at the end of this contract, the incumbent does not successfully re-compete for a contract to continue the work, the nonhuman primates, study specimens, study data, and Government equipment acquired under the contract will need to be moved to the successor SVEU contractor. To provide for this contingency, design and provide to the NIAID Project Officer a Final Transition Plan to coordinate with a successor contractor(s) to achieve an orderly transition of contract resources to the successor contractor. Specify the transition requirements, as well as the methods and time frame for implementing the transition.

a. A **Draft Final Transition Plan** is to be submitted to the NIAID Project Officer and the NIAID Contracting Officer for review and approval two months prior to the completion date of the contract.

b. The **Final Transition Plan** that incorporates all the terms and conditions approved by the NIAID Contracting Officer shall be submitted to the NIAID Project Officer and NIAID Contracting Officer one month prior to the completion date of the contract. The Contractor shall implement the transition plan during the contract's period of performance.

ATTACHMENT TO THE STATEMENT OF WORK

CONFIDENTIALITY OF INFORMATION

Certain information and data provided to the Contractor shall require confidential treatment. Information to be treated confidentially may pertain to proprietary information provided by the AIDS vaccine product and reagent developers and vaccine trial investigators. Primate specimens and HIV- or SIV-specific reagents obtained as a result of this contract shall be restricted to contract-related studies, and shall not be released to any other investigators without approval of the Project Officer(s). All information supplied by the Project Officer(s) should be assumed to be proprietary unless specifically identified as non-confidential in writing by the Project Officer(s). Proprietary data confidentiality will be protected by an Advance Understanding to be included in the contract as follows:

(1) The Contractor agrees that the use of materials provided to the Contractor by or through the Government for studies performed under this project shall be restricted to contract-related projects and shall not be released to any other party without approval of the Project Officer. (2) Because the Contractor may be utilizing and evaluating materials provided to the Government by third parties, including AIDS vaccine product and reagent developers and AIDS vaccine trial investigators, it is essential to include provisions that will protect the rights of these third parties. Therefore the Contractor agrees that manuscripts/abstracts based on data/information generated under this contract will not be submitted for publication until written Project Officer(s) clearance has been received. Contract support shall be acknowledged in all such publications. A "publication" is defined as an issue of printed material offered for distribution or any communication or oral presentation of information.

The Project Officer(s) will review all manuscripts/documents in a period of time not to exceed 30 calendar days from receipt, and will either grant clearance for publication/disclosure, recommend changes or, as applicable, refer the document to the Third Party Supplier of materials utilized under this project for their review.

The NIAID will use its best efforts to assist and expedite the review process by the Third Party Suppliers wherever possible.

INSTRUCTIONS TO OFFERORS FOR THE PREPARATION OF TECHNICAL PROPOSALS AND COST PROPOSALS

INSTRUCTIONS FOR THE STATEMENT OF WORK

1) INITIAL TRANSITION

Note #1 to Offerors: The technical proposal shall include a draft plan and timetable for having the facility ready to start conducting studies.

2) ACQUISITION AND TESTING OF NONHUMAN PRIMATES

Note #2 to Offerors: Discuss your procedures for acquiring nonhuman primates, either from your facility's breeding colonies or from outside sources. If you propose to acquire nonhuman primates from outside sources, identify the primate facilities from which the animals will be purchased and describe and document your past experience in obtaining nonhuman primates from these proposed sources. In addition, discuss your quarantine procedures and the estimated lead time (from past experience) from placement of the order for purchase of the animals to start of study. (The purchase of animals from outside sources is not considered a weakness and will not affect the technical score.) If you propose to acquire nonhuman primates from your own facility, provide a description of the process for transferring animals onto the SVEU.

Note #3 to Offerors: Discuss the macaque species available to you and your experience with these species. Primary emphasis will be on rhesus macaques (Macaca mulatta) of Indian origin. However, because of the continuing shortage of these animals, SVEUs may be requested to house and conduct studies utilizing Chinese-origin rhesus or other nonhuman primate species, such as pig-tail macaques (Macaca nemestrina), cynomolgus monkeys (Macaca fascicularis), African green monkeys (Cercocebus atys), or baboons. Access to baboons, which would be used mainly for immunogenicity studies, may be provided through an arrangement with an off-site facility, but it is not necessary to make actual provisions for baboons in the current proposal, as that can be done at the time that they are needed for a study. In your proposal, indicate which species of nonhuman primates you will have access to through breeding colonies or purchase, and describe your experience in housing the various nonhuman primate species. Discuss plans for, and any relevant issues associated with, housing more than one macaque species concurrently in your facility.

Note #4 to Offerors: For SVEU studies, the Contractor will be required to obtain and provide nonhuman primates that are free of infection with STLV (simian T-cell lymphotrophic virus) and SRV (simian type D retrovirus) in addition to being SIV-free. Provide your procedures for requiring virus testing of animals before purchase and receipt and for repeat testing once the animals are received in your facility to ensure that the animals are free of these infections. Provide similar information on your testing procedures for assuring that the animals are free of tuberculosis.

3) HOUSING AND CARE OF NONHUMAN PRIMATES

Note #5 to Offerors: Provide a description of and relevant documentation for your facility biocontainment procedures for the housing and care of nonhuman primates, especially virus-infected nonhuman primates. Provide documentation describing your training programs for animal care personnel. Attach relevant Standard Operating Procedures (SOPs) in an appendix to your proposal.

Note #6 to Offerors: Provide information describing your animal husbandry practices, environmental enrichment procedures, standard procedures for clinical monitoring and clinical care of nonhuman primates, procedures for the care and clinical monitoring of SIV- and SHIV-infected animals, procedures for performance of surgical procedures and post mortems, criteria for recommending euthanasia, and procedures for euthanasia. Attach relevant SOPs in an appendix to your proposal.

Note #7 to Offerors: Provide information describing your experience in housing and caring for nonhuman primates for vaccine studies and other studies as specified in the SOW.

Note #8 to Offerors: Provide documentation of Office of Laboratory Animal Welfare (OLAW) assurance and your assurance number, documentation of Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC) accreditation, and information about the composition, expertise, experience, and regulations of your Institutional Animal Care and Use Committee (IACUC).

Note #9 to Offerors (BUDGET): The approximate number of nonhuman primates to be housed at an SVEU is expected to range from approximately 100 per site up to approximately 300 per site, depending upon the available capacity of the facility, experience of the Offeror's personnel in conducting vaccine studies, the outcome of the review of proposals, and needs of NIAID. The initial proposal should be based on the number of nonhuman primates that the Offeror would be able and willing to make available to NIAID for studies to be conducted under this contract.

For purposes of this proposal, Offerors are requested to submit two budgets: First, Offerors are requested to submit a proposed seven year budget covering the costs of the number of nonhuman primates that they would be able and willing to make available to NIAID for studies to be conducted under this contract. Year 1 of this budget should include the purchase cost of nonhuman primates needed to reach the Offeror's proposed capacity. After Year 1, Offerors should budget for the purchase of 50-150 nonhuman primates per year, depending upon the proposed capacity of the contract. (Although Offerors would be expected to be able to house, on-site, the agreed-upon 100-300 animals, there will not be a turnover of that number of animals per year. Therefore, it is not expected that Offerors will purchase the full complement of animals each year. However, because it is often necessary to purchase young animals and hold them until they are large enough to use, or because there is often a need to purchase animals when they are available, even if there is not space at the SVEU facility, Offerors should budget for the 50-150 animal per year purchase, because animals can be housed off-site until ready for use in a study at the SVEU facility.)

Secondly, **for purposes of providing a uniform basis of comparison among proposals**, Offerors are requested to prepare a partial second budget presenting only their Year 1 costs to maintain a population of 100 nonhuman primates for the conduct of vaccine/vaccine-related studies.

Note #10 to Offerors (BUDGET): For Offerors proposing to acquire nonhuman primates from outside sources, include current purchase cost estimates in the business proposal. For Offerors proposing to acquire nonhuman primates from their own facility, include the costs for transferring animals into the SVEU in the business proposal.

4) PROTOCOL DEVELOPMENT

Note #11 to Offerors: Provide relevant documentation of your experience in designing study protocols for SIV, SHIV, or HIV vaccine studies, for *in vivo* titrations of virus challenge stocks, for microbicide studies, and for other relevant studies described in the SOW, and describe your experience in collaborating with investigators in the design and conduct of the study protocols.

5) CONDUCT OF STUDIES

Note #12 to Offerors: Discuss your procedures for, and experience with, the conduct of: vaccine studies, *in vivo* virus titrations, route of immunization/route of infection studies, microbicide studies, generation of virus stocks, antiviral therapy, and immunotherapy studies in nonhuman primates, including immunization by various routes, sample collection (blood, muscosal, tissue), and virus challenges, with attention to the elements of the SOW outlined under this section. Provide relevant SOPs in an appendix to your proposal.

Note #13 to Offerors: Provide descriptions of biocontainment procedures and safety precautions to be observed during virus inoculation, blood and tissue collection, shipping of biohazardous samples, disposal of biohazard waste, etc. In an appendix to your proposal, provide your Institutional SOPs for these biosafety procedures and the SOPs for training of the personnel who will be providing these functions.

Note #14 to Offerors (BUDGET): For budgetary purposes, it is anticipated that serum and lymphocytes will be collected, processed, and stored on the average of twice a month from each animal entered into an experimental vaccine protocol. Mucosal samples are anticipated to be collected monthly during a study (assume 12 months). Procedures for collection of lymph node biopsies are anticipated to be performed on the average of once a year per animal (assume 25 monkeys per year), and procedures for mucosal (vaginal or rectal) biopsies are anticipated to be collected on the average of twice a year per animal (assume 50 monkeys per year). CD4 counts and total

lymphocyte counts, as well as standard clinical blood chemistries are to be done on all the animals on a regular basis, and CD4 counts/total lymphocyte counts are to be done at least monthly on animals after viral challenge. It is anticipated that the currently available panel of MHC assays will be conducted on all the rhesus macaques used for studies. (MHC typing of other species may be required in the future, but the assays are not now available.)

Note #15 to Offerors (BUDGET): For budgetary purposes, assume that 100 animals will be infected with virus per year. It is anticipated that plasma, serum and lymphocytes will be collected and processed six times in the first month following virus challenge, twice a month from each animal for the next six months, then monthly for the duration of the study (estimate: 12 months). Procedures for collection of lymph nodes are anticipated to be performed on the average of six times per year. For purposes of cost estimates, Offerors should estimate the cost of 20 necropsies per year.

6) *IN VITRO* LABORATORY IMMUNOLOGIC AND VIROLOGIC ASSAYS

Note #16 to Offerors: Describe your biocontainment procedures for handling and disposing of biohazardous virus-containing materials and samples from virus-infected animals. Provide documentation of your biosafety training programs for your laboratory personnel. Include relevant SOPs in an appendix to your proposal.

Note #17 to Offerors: Because the NIAID has separate, non-SVEU contractors who will conduct the majority of assays for cellular immune responses and the assays to detect and characterize neutralizing antibodies, the SVEUs are expected to focus mainly on the conduct of ELISA and western blot assays to detect antiviral antibodies in immunized and/or infected animals. However, if you have the expertise to provide additional assays, they may be included in the proposal. Describe the immunologic analyses you are proposing to conduct to assess the immunological responses of immunized animals and of challenged/infected animals. Discuss your use of appropriate controls and quality control of assays, and include SOPs where possible. Provide experimental data from previous studies demonstrating your experience with the assays. Discuss procedures you would use to compare assays with the NIAID Primate Immunology Laboratory and other SVEUs or to train personnel to conduct new assays.

Note #18 to Offerors: Although the NIAID has a separate contractor to perform assays to detect plasma virus RNA in challenged and infected macaques, if specified in the study protocol, the SVEUs may be requested to perform virologic analyses of specimens from animals at multiple times after challenge with SIV, SHIV, or HIV. Although it is anticipated that most, if not all, assays for plasma viral RNA will be conducted by the Primate Virology Laboratory, you may be requested to confirm infection by detecting viral RNA or DNA in tissues such as peripheral blood lymphocytes or lymph nodes, or to conduct virus isolation by co-cultivation of the nonhuman primate tissue with appropriate target cells. You will be requested to conduct *in vitro* titrations, especially on virus stocks used for challenges. In this section of your proposal, describe the assays you are proposing to perform. Discuss your use of appropriate controls and quality control of assays and include SOPs where possible. Provide experimental data from previous studies demonstrating your experience with the assays. Discuss procedures you would use to compare assays with the NIAID Primate Virology Laboratory and other SVEUs or to train personnel to conduct new assays.

Note #19 to Offerors (BUDGET): Because Offerors are requested to demonstrate the capability to conduct ELISA assays and immunoblotting (Western blot) assays and may propose to conduct one or more additional assays to assess immunological responses, for purposes of this proposal Offerors shall propose to conduct ELISA assays on 12 serum samples per year per monkey, and Western blot on 12 samples per year per monkey. Offerors proposing to conduct other assays in addition shall budget for performing 100 (total) of each type of proposed assay per year.

Note #20 to Offerors (BUDGET): Because Offerors are requested to demonstrate the capability to conduct *in vitro* virus titrations, as well as virus isolation, and may propose to conduct plasma virus RNA assays and other assays to assess the virological status of challenged animals, for purposes of this proposal, Offerors are requested to propose to conduct virus isolation by co-cultivation with appropriate target cells on an average of 2 samples per year per monkey for 50 monkeys per year. For purposes of cost estimates for this proposal, Offerors proposing to conduct plasma virus RNA assays should assume that they will conduct 30 assays per year per monkey for 50 monkeys per year. Offerors proposing to conduct other assays should assume that they will conduct assays on 5 samples per year per monkey for 50 monkeys.

7) STORAGE AND SHIPMENT OF MATERIALS

Note #21 to Offerors: Describe your procedures for storage of materials at -20°C and -80°C (as appropriate for the sample being stored), and your procedures for monitoring of storage conditions. Describe your sample inventory system.

Note #22 to Offerors: Describe your procedures for the shipment of specimens (plasma, serum, fresh cells, frozen cells, etc.), with emphasis on your procedures for shipment of biohazardous material.

Note #23 to Offerors: (BUDGET) For purposes of this proposal, Offerors should estimate the cost of 18 shipments per year of fresh peripheral blood cells or other tissue to Boston, MA. (to the Cellular Immunology Laboratory), 12 shipments per year to Durham, NC. (to the Neutralizing Antibody Assay Laboratory), and 12 shipments per year to Kensington, MD. (to the Viral RNA Assay Laboratory).

8) ENTRY OF SVEU STUDY PROTOCOLS, INFORMATION, AND DATA INTO THE DAIDS SVEU DATABASE

Note #24 to Offerors: The DAIDS database for SVEU vaccine studies will be an integral part of the conduct of studies. Describe your plans for personnel, computer capability, and procedures for entering study data into the database and for ensuring the accuracy of the data entered.

Note #25 to Offerors: Appendix B contains sample screens from the database to give Offerors an example of the information from the study protocols that will be entered into the database.

Note #26 to Offerors: (BUDGET) Because of the requirement for entry of study protocols and data into the DAIDS SVEU Database, Offerors are requested to budget for personnel to perform this function. The designated person or persons may be the Study Coordinator or other personnel already included on the contract, or may be an additional person, preferably someone with computer experience. While the amount of time needed for this function will vary, an average of 10% -20% of an FTE per week should be sufficient. The DAIDS SVEU Database, which is an Oracle web-based system, will be maintained by a separate NIAID contractor (not the SVEUs), and the database server web site will be accessible via email.

9) COMMUNICATIONS WITH THE NIAID PROJECT OFFICER

Note #27 to Offerors: Describe your proposed procedures for communicating study data and results to the NIAID Project Officer, as outlined in the SOW.

Note #28 to Offerors: (BUDGET) For purposes of this proposal, Offerors should estimate the cost of one trip to NIH, Bethesda, Maryland per year for two investigators for a two day meeting, and the cost of travel to one domestic AIDS vaccine-related scientific meeting per year for each of two investigators.

10) FINAL TRANSITION

Note #29 to Offerors: If the Offeror is not awarded a contract to continue as an SVEU at the end of this contract there will be a need to move nonhuman primates, frozen samples, study data, and any Government equipment to the new contractor. Provide a draft plan for such a transition, including the movement of SIV- or SHIV- infected animals that may remain on study in your facility.

INSTRUCTIONS FOR PERSONNEL

Note #30 to Offerors: Because of the importance of experienced personnel in the conduct of the SVEU studies, your proposal should provide thorough descriptions of the capabilities and experience of proposed personnel. In addition, provide an organizational chart that demonstrates how the proposed personnel fit into the overall organization and that clearly defines lines of supervision and responsibility.

1) For Principal Investigator:

   Thoroughly describe and document the experience and qualifications of the Principal Investigator (PI). Indicate the percentage of effort the PI will commit to the management of the SVEU projects. Describe the PI's past experience in the management/direction of multiple simultaneous studies and past experience in supervising the conduct of AIDS vaccine studies in nonhuman primates. Also include a curriculum vita for the PI.

2) Veterinary, animal technician, and animal care staff:

   Thoroughly describe and document the experience and qualifications of veterinarians and senior veterinary personnel. Describe and document their experience that relates to the conduct of the relevant aspects of the SOW. Indicate the percentage of effort each is expected to commit to the contract. Describe the experience of additional animal technician and animal care staff in the care of nonhuman primates with emphasis on their experience with virus-infected animals. Indicate the percentage effort each will commit to the contract.

3) Scientific staff and technical laboratory staff:

   Thoroughly describe and document the experience and qualifications of scientific staff and technical laboratory personnel. Describe and document their experience as it relates to the conduct of the relevant aspects of the SOW. Indicate the percentage of effort each is expected to commit to the project and define their responsibilities related to the conduct of SVEU studies. Also provide CVs for the scientific personnel. It is not necessary to provide CVs for laboratory technical personnel, but a thorough description of their expertise and experience should be included, and their responsibilities on the SVEU contract should be clearly defined.

4) Study Coordinator:

   A Study Coordinator, who will be responsible for the day-to-day management and coordination of SVEU studies, including coordination entry of data into the DAIDS SVEU Database and coordination of shipping and storage of samples, is essential to the contract. Provide a description of the qualifications and experience of the proposed Study Coordinator. Describe how the proposed Study Coordinator will interact with other personnel to assure effective and efficient conduct of the studies.

INSTRUCTIONS FOR FACILITIES AND RESOURCES

Note #31 to Offerors: Discuss the availability of facilities, equipment, and other resources necessary for the conduct of this project. Include the floor plan of the proposed facility and list equipment and resources available to the project. Confirm that the facility will be available at the time of Contract award and during the period of performance of the Contract.

Note #32 to Offerors: Document the availability of, and provide a description of, appropriate (BSL2 with BSL3 practices) biocontainment facilities for housing nonhuman primates infected with SIV, SHIV, or HIV. Document the availability of, and provide a description of, appropriate (BSL2) biosafety laboratory facilities for handling virus and processing blood and other tissues from virus-infected animals and for conducting the immunological and virological assays outlined in the SOW.

INSTRUCTIONS FOR SECTION 4: OTHER INFORMATION

Because of the need to conduct cellular immunological assays on fresh, unfrozen peripheral blood lymphocytes at the NIAID Primate Cellular Immunology Laboratory within a few hours of collection from nonhuman primates in vaccine studies, an SVEU contract will only be awarded to Offerors with primary facilities in the continental United States. However, a U.S. site may propose foreign subcontract sites if such sites would enhance the scientific performance of the contract and if such sites are proposed only for studies that do not require the conduct of cellular immunological assays (such as microbicide studies). If a foreign subcontract site is proposed, the facilities, equipment, and qualifications of the staff must be provided for evaluation, and must be of sufficient quality to ensure the integrity of studies proposed to be conducted there. If subcontractors are proposed, the same information as required in Sections 1 through 3 above should be provided for each subcontractor.

REPORTING REQUIREMENTS AND DELIVERABLES

A. Entry of study information and data into the DAIDS SVEU Database

Protocols, data and information pertaining to SVEU vaccine studies are to be entered into the DAIDS SVEU Database in an on-going and timely manner to allow efficient conduct of the studies. Provide a monthly email update to the NIAID Project Officer, describing the status of entry of each approved protocol into the DAIDS SVEU Database and the status of entry of data for each immunization, sample collection, and challenge time point for each protocol.

B. Deliverables

Within 2 weeks after contract award, the Contractor shall submit a contract specific information security plan for review and approval by NIAID.

Protocols for vaccine studies and other studies are to be developed and provided to the NIAID Project Officer on an on-going and timely manner to allow efficient conduct of the studies.

Data and other information from SVEU studies, including clinical data and information about SVEU animals, are to be provided to the NIAID Project Officer upon request.

Copies of Standard Operating Procedures (SOPs) are to be provided to the NIAID Project Officer upon request.

Samples from studies conducted under this contract, or reagents connected with the studies, are to be delivered (in lieu of delivery to NIAID directly) to third parties as specified in the study protocol or as directed by the NIAID Project Officer.

Before the end of the contract, if the Contractor is not awarded a subsequent contract to continue as an SVEU site, all nonhuman primates, study data and animal records, frozen samples from studies, vaccines, virus stocks, Government equipment, and any other materials considered to be part of the contract are to be delivered to the new SVEU contractor according to the Final Transition Plan required by the SOW.

The Initial Transition Plan, Draft Final Transition Plan, and the Final Transition Plan are to be delivered to the Project Officer and to the Contracting Officer at the times described in SOW Sections 1 and 10.

C. Technical Reports

In addition to those reports described above, the Contractor shall prepare and submit the following written reports in the manner stated below. The reports shall also be submitted to the NIAID Project Officer and Contracting Officer in electronic version.

1. Single Trial Final Report - Within 6 weeks after the close of a vaccine candidate evaluation, the Contractor shall submit a final report of that study. Four (4) copies of the report shall be submitted to the NIAID Project Officer. This report shall include the purpose of the trial, the product tested, the protocol for the study, and a summary of data from the study.

2. Semi-annual Progress Reports - By the fifteenth working day of the month following the end of each reporting period, the Contractor shall submit five (5) copies of a semi-annual progress report, comprising four (4) copies to the NIAID Project Officer and one (1) copy to the NIAID Contracting Officer, which consists of the following:

    (a) A title page containing:

        1) Contract number and title

        2) Sequence of report, e.g. - "Year 1, Second Semi-annual Report"

        3) Period of performance covered

4) Contractor's name and address

5) Date of submission

(b) Reports shall include at a minimum the following information:

1) Section A - An introduction covering the purpose and scope of the contract effort and listing the studies covered in the report.

2) Section B – This section should be divided into separate reports for each study conducted under the contract. **The report for each study shall be a continuous, running report,** starting with the title of the study, names of collaborators, the protocol outline and a description of the study. This shall be followed by the status of the study at each prior reporting period, with an update for the current period. The report shall include information about any immunization or virus challenge, or other treatment that the animals received during the current reporting period, including the date and study week of the treatment. The report shall include the dates of sample collection and a list of the assays to be conducted on these samples. If the assays are conducted by the SVEU, the report shall include pertinent data and/or graphs in sufficient detail to follow the progress of individual animals through the phases of a vaccine experiment. If the assays are conducted by the Primate Immunology Laboratory or by another investigator, this shall be indicated, including the dates samples were shipped to the other laboratory, and any data that was sent back to the SVEU from other laboratories. The report shall include an overview of information about the health status of the animals, especially CD4 status and virus load status after challenge, and shall report any deaths of animals and the causes of death. The report shall include any other relevant information about the study, including decisions that were reached about future plans for the study.

3) Section C – This section shall list the number of animals in each study and the total number of animals on the contract as of the end of each reporting period.

4) Section D – This section shall include a description of any technical or performance problems encountered and corrective actions planned or taken. An explanation of any differences between planned and actual progress shall be included.

5) A semi-annual report will not be required when an annual report is due.

3. Annual Report - On or before the last day of the Contract year, the Contractor shall submit five (5) copies of an annual report. Four (4) copies shall be submitted to the NIAID Project Officer and one (1) copy shall be submitted to the NIAID Contracting Officer. The annual report shall summarize progress for the entire Contract year, using the same format described for Semi-annual Progress Reports. Any individual study reports previously submitted during the year shall also be included in the annual report.

4. Final Contract Report - The Contractor shall submit five (5) copies of the final report; four (4) copies shall be submitted to the NIAID Project Officer and one (1) copy shall be submitted to the NIAID Contracting Officer. The final report shall summarize the results of the entire contract work for the period of performance covered. This report shall be in sufficient detail to comprehensively explain the results achieved and shall be submitted two weeks prior to the completion date of the Contract to allow time for any revisions before the contract period of performance expires.

The Final Contract Report shall contain:

a. Title Page as described above in paragraph A.2. (a)
b. Introduction covering the purpose and scope of the contract effort.
c. Description of the overall progress, plus a separate description of each study on which effort was expended during the period of performance. Descriptions will include pertinent data to present significant results achieved and a scientific evaluation of the data accrued under the contract.

5. If the Contractor becomes unable to deliver the specified reports within the period of performance because of unforeseen difficulties, notwithstanding the exercise of good faith and diligent efforts in performance of

the work, the Contractor shall give the NIAID Contracting Officer immediate written notice of anticipated delays with reasons therefore. If the NIAID Contacting Officer and NIAID Project Officer approve the extension, they will work with the Contractor to establish a new delivery date.

D. Technical Report Distribution

Copies of the technical reports shall be submitted as follows:

Type of Report	Number of Copies	Due Date
Single Trial Final	4 copies –NIAID PO	Due six weeks after completion of the study.
Semi-Annual Progress	Original –NIAID CO 4 copies -NIAID PO	Due on or before the 15th of the month following each semi-annual reporting period. Not due when Annual or Final reports are due.
Annual	Original –NIAID CO 4 copies –NIAID PO	Due on or before the 30th of the month following each Anniversary date of the contract.
Final	Original –NIAID CO 4 copies –NIAID PO	Due two weeks before the completion date of the contract.

E. Addresses:

Project Officer:
Project Officer,
PRDB, VPRP, DAIDS, NIAID, NIH
6700-B Rockledge Drive
Bethesda, MD 20892-7624

Contracting Officer:
Contracting Officer
Contract Management Program
DEA, NIAID, NIH
6700-B Rockledge Drive
Bethesda, MD 20892-7612

Other deliverables as described in paragraph B. above are due as indicated.

PART I - THE SCHEDULE

SECTIONS B - H -- UNIFORM CONTRACT FORMAT - GENERAL

A Sample Uniform Contract Format may be found at the following website:

http://rcb.cancer.gov/rcb-internet/wkf/sample-contract.htm

PART II – CONTRACT CLAUSES

SECTION I - CONTRACT CLAUSES

THE FOLLOWING PAGES CONTAIN A LISTING(S) OF GENERAL CLAUSES WHICH WILL BE APPLICABLE TO MOST CONTRACTS RESULTING FROM THIS RFP. HOWEVER, THE ORGANIZATIONAL STRUCTURE OF THE SUCCESSFUL OFFEROR(S) WILL DETERMINE THE SPECIFIC GENERAL CLAUSES LISTING TO BE CONTAINED IN THE CONTRACT(S) AWARDED FROM THIS RFP.

ARTICLE I.1. GENERAL CLAUSES

The complete listing of these clauses may be accessed at: http://rcb.cancer.gov/rcb-internet/appl/general-clauses/clauses.jsp

The following General Clause Listings will be applicable to most contracts resulting from this RFP. However, the organizational structure of the successful offeror(s) will determine the specific General Clause Listing to be contained in the contract(s) awarded from this RFP:

General Clauses for a Cost-Reimbursement Research and Development Contract

ARTICLE I.2. AUTHORIZED SUBSTITUTIONS OF CLAUSES

ITEM 3: FAR Clause **52.215-15**, **Pension Adjustments and asset Reversions** (OCTOBER 2004), FAR Clause 52.215-18, **Reversion or Adjustment of Plans for Post Retirement Benefits (PRB) other than Pensions** (OCTOBER 1997) and 52.215-19, **Notification of Ownership Changes** (OCTOBER 1997), are deleted in their entirety.

ITEM 4: **ALTERNATE IV** (OCTOBER 1997) of FAR Clause **52.215-21, Requirements for Cost or Pricing Data or Information Other than Cost or Pricing Data--MODIFICATIONS** (OCTOBER 1997) is added.

ITEM 9: **Alternate II** (OCTOBER 2001) of FAR Clause **52.219-9, Small Business Subcontracting Plan** (JANUARY 2002) is added.

No additional or supplemental Authorized Substitutions of Clauses are applicable to this solicitation. See **I.2 Authorized Substitutions of Clauses** of SECTION I at http://rcb.cancer.gov/rcb-internet/wkf/sectioni.pdf for the general listing of Authorized Substitutions of Clauses.

ARTICLE I.3. ADDITIONAL CONTRACT CLAUSES

ITEM 39: FAR Clause **52.219-25, Small Disadvantaged Business Participation Program--Disadvantaged Status and Reporting** (OCTOBER 1999), is applicable to this solicitation.

ITEM 59: FAR Clause **52.237-3, Continuity of Services** (JANUARY 1991), is applicable to this solicitation.

No additional or supplemental Additional Contract Clauses are applicable to this solicitation. See **I.3 Additional Contract Clauses of** SECTION I at http://rcb.cancer.gov/rcb-internet/wkf/sectioni.pdf for the general listing of Additional Contract Clauses.

ARTICLE I.4. ADDITIONAL FAR CONTRACT CLAUSES INCLUDED IN FULL TEXT:

No additional or supplemental Additional FAR Contract Clauses Included in Full Text are applicable to this solicitation. See **I.4. Additional FAR Contract Clauses Included in Full Text** of SECTION I at http://rcb.cancer.gov/rcb-internet/wkf/sectioni.pdf for the general listing of Additional FAR Contract Clauses Included in Full Text.

PART III - LIST OF DOCUMENTS, EXHIBITS AND OTHER ATTACHMENTS

SECTION J - LIST OF ATTACHMENTS

The following Attachments are provided in full text with this Solicitation:

PACKAGING AND DELIVERY OF PROPOSALS: (http://www.niaid.nih.gov/contract/eproposal.htm#pack)

HOW TO PREPARE AN ELECTRONIC PROPOSAL: (http://www.niaid.nih.gov/contract/eproposal.htm#electronic)

PROPOSAL INTENT RESPONSE SHEET SUBMIT ON/BEFORE: July 10, 2005 (Attached to this listing)

[NOTE: Your attention is directed to the "Proposal Intent Response Sheet". If you intend to submit a proposal, you should complete this form and return it to this office via fax or e-mail on or before the date identified above. The receipt of this form is critical as it contains information essential for CMP's coordination of the electronic submission and review of proposals.]

RFP FORMS AND ATTACHMENTS:

THE RFP FORMS/ATTACHMENTS LISTED BELOW ARE AVAILABLE IN A VARIETY OF FORMATS AND MAY BE VIEWED OR DOWNLOADED DIRECTLY FROM THIS SITE:

http://www.niaid.nih.gov/contract/forms.htm

APPLICABLE TO TECHNICAL PROPOSAL (INCLUDE THESE DOCUMENTS/FORMS WITH YOUR TECHNICAL PROPOSAL):

- **Technical Proposal Cover Sheet**
- **NIH-1688-1, Project Objectives**
- **Technical Proposal Cost Information**
- **Summary of Related Activities**
- **Government Notice for Handling Proposals**

APPLICABLE TO BUSINESS PROPOSAL (INCLUDE WITH YOUR BUSINESS PROPOSAL):

- **NIH-2043, Proposal Summary and Data Record**
- **Small Business Subcontracting Plan Format**
- **Breakdown of Proposed Estimated Cost (plus fee) and Labor Hours**
- **Offeror's Points of Contact**

TO BECOME CONTRACT ATTACHMENTS (INFORMATION ONLY):

- **NIH(RC)-4: Invoice/Financing Request and Contract Financial Reporting Instructions for NIH Cost-Reimbursement Type Contracts**
- **NIH(RC)-7: Procurement of Certain Equipment, (OMB Bulletin 81-16)**
- **Safety and Health, HHSAR Clause 352.223-70**
- **Report of Government Owned, Contractor Held Property**
- **Government Property Schedule**
- **Disclosure of Lobbying Activities, OMB Form LLL**

PART IV – REPRESENTATIONS AND INSTRUCTIONS

SECTION K - REPRESENTATIONS, CERTIFICATIONS AND OTHER STATEMENTS OF OFFERORS

Representations, Certifications, and Other Statements of Offerors or Quoters (Negotiated).

1. REPRESENTATIONS AND CERTIFICATIONS

The Representations and Certifications required by this particular acquisition can be accessed electronically from the INTERNET at the following address:

http://rcb.cancer.gov/rcb-internet/wkf/sectionk.pdf

If you are unable to access this document electronically, you may request a copy from the Contracting Officer identified on the cover page of this solicitation.

IF YOU INTEND TO SUBMIT A PROPOSAL, YOU MUST COMPLETE THE REPRESENTATIONS AND CERTIFICATIONS AS PART OF YOUR ORIGINAL BUSINESS PROPOSAL. ADDITIONALLY, REPRESENTATIONS AND CERTIFICATIONS MUST ALSO BE COMPLETED FOR ANY PROPOSED SUBCONTRACTORS.

SECTION L - INSTRUCTIONS, CONDITIONS, AND NOTICES TO OFFERORS

The following information is specific to this solicitation and is provided to supplement and/or complete the associated ITEMS presented at the SECTION L website at http://rcb.cancer.gov/rcb-internet/wkf/sectionl.pdf

I. GENERAL INFORMATION

ITEM 2: **Alternate I, of FAR Clause 52.215-1, INSTRUCTIONS TO OFFERORS-COMPETITIVE ACQUISTION,** is applicable to this solicitation.

ITEM 9: **NAICS CODE AND SIZE STANDARD**

Note: The following information is to be used by the offeror in preparing its Representations and Certifications (See Section K of this RFP), specifically in completing the provision entitled, **SMALL BUSINESS PROGRAM REPRESENTATION,** FAR Clause 52.219-1.

(1) The NAICS Code is 541710
(2) The small business size standard is 500 employees.

ITEM 10: **THIS REQUIREMENT IS NOT SET ASIDE FOR SMALL BUSINESS,** is applicable to this solicitation.

ITEM 11: **TYPE OF CONTRACT AND NUMBER OF AWARD(S)**

It is anticipated that multiple awards will be made from this solicitation and that the awards will be made on/about May 8, 2006.

It is anticipated that the awards from this solicitation will be multiple-year cost reimbursement completion contracts with a period of performance of seven years, and that incremental funding will be used [see Section L, PART IV - Business Proposal Instructions].

ITEM 13: **ESTIMATE OF EFFORT**

It is expected that a completion type contract will be awarded as a result of this RFP. To assist you in the preparation of your proposal, the Government considers the effort to be approximately 14,872 labor hours per year. This information is furnished for the offeror's information only and is not to be considered restrictive for proposal purposes.

ITEM 16: **COMPARATIVE IMPORTANCE OF PROPOSALS**

You are advised that paramount consideration shall be given to the evaluation of technical proposals. All evaluation factors other than cost or price, when combined, are significantly more important than cost or price. The relative importance of the evaluation factors is specified in SECTION M of this solicitation. However, the Government reserves the right to make an award to the best advantage of the Government, cost and other factors considered.

ITEM 20: **LATE PROPOSALS AND REVISIONS,** HHSAR 352.215-70, is applicable to this solicitation.

II. GENERAL INSTRUCTIONS

ITEM 23: **Potential Award Without Discussions,** is applicable to this solicitation.

ITEM 26: **Care of Live Vertebrate Animals,** is applicable to this solicitation.

ITEM 29: **Sharing Research Data,** is applicable to this solicitation.

ITEM 33: **Small Business Subcontracting Plan,** is applicable to this solicitation and the following information is provided to supplement this item to assist in proposal preparation:

The anticipated minimum subcontracting goals for this RFP are as follows:

23% for Small Business; 5% for Small Disadvantaged Business; 5% for Women-Owned Small Business; 5% for HUBZone Small Business; and 3% for Veteran-Owned Small Business and 3% for Service-Disabled Veteran-Owned Small Business.

ITEM 35: **Extent of Small Disadvantaged Business Participation,** is applicable to this solicitation.

ITEM 36: **Salary Rate Limitation in Fiscal Year 2005,** is applicable to this solicitation.

ITEM 39: **Past Performance Information**

(a) Offerors shall submit the following information as part of their **BUSINESS** proposal.

A list of the last five (5) contracts completed during the past three years and all contracts currently in process that are similar in nature to the solicitation workscope.

Include the following information for each contract or subcontract:

1. Name of Contracting Organization
2. Contract Number (for subcontracts, provide the prime contract number and the subcontract number)
3. Contract Type
4. Total Contract Value
5. Description of Requirement
6. Contract Officer's Name and Telephone Number
7. Program Manager's Name and Telephone Number
8. Standard Industrial Code

The Offeror shall submit comparable information on all subcontractors that the offeror proposes to perform a major subcontract under this effort. For the purpose of this solicitation, a "major subcontract" is defined as subcontracts over $500,000. The Offeror may provide information on problems encountered on the identified contracts and the offeror's corrective actions.

(b) Each offeror will be evaluated on its performance under existing and prior contracts for similar products and services. The Government is not required to contact all references provided by the offeror. Also, references other than those identified by the offeror may be contacted by the Government to obtain additional information that will be used in the evaluation of the offeror's past performance.

ITEM 48: **Prohibition on Contractor Involvement with Terrorist Activities**, is applicable to this solicitation.

ITEM 49: **Solicitation Provisions Incorporated by Reference:** The following provisions are applicable to this solicitation.

Submission of Offers in the English Language, FAR Clause 52.214-34, (April 1991).

Submission of Offers in U.S. Currency, FAR Clause 52.214-35, (April 1991).

Facilities Capital Cost of Money, FAR Clause 52.215-16, (October 1997).

Order of Precedence-Uniform Contract Format, FAR Clause 52.215-8, (October 1997).

Data Universal Numbering System (DUNS) Number, FAR Clause 52.204-6, (October 2003).

III. TECHNICAL PROPOSAL INSTRUCTIONS

ITEM 51: **Project Objectives, NIH-1688-1, is** applicable to this solicitation.

IV. BUSINESS PROPOSAL INSTRUCTIONS

ITEM 56: **Proposal Cover Sheet,** is applicable to this solicitation.

ITEM 60: **Requirement for Cost or Pricing Data or Information Other than Cost or Pricing Data [FAR Clause 52.215-20 (October 1997)],** is applicable to this solicitation.

ITEM 65: **Incremental Funding,** is applicable to this solicitation.

SECTION M - EVALUATION FACTORS FOR AWARD

1. GENERAL

Selection of an Offeror for contract award will be based on an evaluation of proposals against four factors. The factors in order of importance are: technical, cost/price, past performance and Small Disadvantaged Business (SDB) participation. Although technical factors are of paramount consideration in the award of the contract, cost/price, past performance and SDB Participation are also important to the overall contract award decision. All evaluation factors other than cost/price, when combined, are significantly more important than cost or price. The trade-off process described in FAR 15.101-1 may be employed. This process permits tradeoffs among cost/price and non-cost factors and allows the Government to consider award to other than the lowest priced or highest technically rated Offeror. In any event, the Government reserves the right to make an award(s) to that Offeror whose proposal provides the best overall value to the Government.

The evaluation will be based on the demonstrated capabilities of the prospective Contractors in relation to the needs of the project as set forth in the RFP. The merits of each proposal will be evaluated carefully. Each proposal must document the feasibility of successful implementation of the requirements of the RFP. Offerors must submit information sufficient to evaluate their proposals based on the detailed criteria listed below.

2. EVALUATION OF DATA SHARING PLAN

The Offeror's plan for the sharing of final research data shall be assessed for appropriateness and adequacy. If your proposal does not include a plan or if the plan in your proposal is considered "unacceptable," you will be afforded the opportunity to further discuss, clarify or modify your data sharing plan during discussions and in your Final Proposal Revision (FPR). If your data sharing plan is still considered "unacceptable" by the Government after discussions, your proposal may not be considered further for award.

3. MANDATORY EVALUATION CRITERIA

Because of the need to conduct cellular immunological assays on fresh, unfrozen peripheral blood lymphocytes at the NIAID Primate Cellular Immunology Laboratory within a few hours of collection from nonhuman primates in vaccine studies, an SVEU contract will be awarded only to Offerors with primary facilities in the continental United States. Proposals received from non-continental U.S. Offerors will be excluded from further evaluation and will not be considered for award.

4. TECHNICAL EVALUATION CRITERIA

The evaluation criteria are used by the technical evaluation committee when reviewing the technical proposals. Proposals will be judged solely on the written material provided by the Offeror. The criteria below are listed in the order of relative importance with weights assigned for evaluation purposes.

CRITERIA (100 POINTS TOTAL)

A. PERSONNEL: **(40 points)**

Strength and adequacy of the documented experience, expertise, and availability of scientific, technical, and veterinary staff, with emphasis on the experience and expertise of the proposed staff in the conduct of SIV and/or HIV vaccine studies in nonhuman primate models, and experience in handling SIV-infected, SHIV-infected, or HIV-infected nonhuman primates.

1) Strength and adequacy of the experience, expertise, and availability of the Principal Investigator in the conduct and management/direction of SIV or HIV vaccine studies, particularly in the management of multiple simultaneous studies. **10 points**

2) Strength and adequacy of the experience, expertise, and availability of veterinary, animal technicians, and animal care staff. Demonstrated experience with proposed procedures for animal husbandry, immunization, blood sample collection, virus inoculation, and other tasks related to conducting studies using nonhuman primates, as outlined in the Statement of Work. **10 points**

3) Strength and adequacy of the experience, expertise, and availability of scientific and technical staff. Strength and adequacy of the demonstrated experience with the assays proposed to conduct immunological, virological, other laboratory tasks, and DAIDS SVEU Database duties outlined in the Statement of Work. **10 points**

4) Strength and adequacy of the experience and availability of the proposed Study Coordinator who will be responsible for the day-to-day management of the components of the protocol, the receipt and shipping and storage of samples related to the studies conducted under this contract, and the reporting of the status of studies to the NIAID Project Officer on an ongoing basis. **10 points**

B. TECHNICAL APPROACH/METHODOLOGY: **(40 points)**

Merit, feasibility, and thoroughness of the proposed methodology and technical approach to conduct the elements of the Statement of Work including:

1) The proposed procedures for animal husbandry, immunization, blood sample collection, virus inoculation, and other tasks related to conducting studies using nonhuman primates, as outlined in the Statement of Work. The proposed procedures and precautions used in dealing with virus-infected animals. **15 points**

2) The proposed methodology, including biocontainment precautions, to be used to process samples and to conduct immunological assays to assess the animals' responses to immunization and infection. The proposed methodology, including biocontainment precautions, to be used to process samples from virus-inoculated animals and to conduct virus isolation and other assays for virus detection or quantitation. **15 points**

3) The proposed plans for project management, including an organizational chart; proposed plans for staff training, including biohazard training; proposed procedures for entry of SVEU study protocols, data, and information into the DAIDS SVEU Database; proposed procedures for storage of study samples and materials, including freezer back-up systems; proposed procedures for shipment of study samples, including shipping of samples from virus-infected animals; proposed procedures for communication with the NIAID Project Officer; proposed plans for turnover to a new contractor, if necessary, at the end of the contract. **10 points**

C. RESOURCES AND FACILITIES: **(20 points)**

1) Merit, adequacy, and documented availability of appropriate (BSL2 and BSL2/BSL3 practices) biocontainment facilities for housing and conducting studies with uninfected, SIV-infected, SHIV-infected, or HIV-infected nonhuman primates; documented availability of appropriate (BSL2) biosafety laboratory facilities for handling virus as well as blood and other tissues from uninfected and from virus-infected animals, for conducting immunological assays, for culturing and handling virus, and for conducting virological assays. **10 points**

2) Merit and adequacy of proposed plans for acquisition of nonhuman primates, including a description of any current, established source of nonhuman primates, any past history of sources previously used, and the proposed sources to be used to acquire nonhuman primates for the studies to be conducted. **10 points**

5. PAST PERFORMANCE FACTOR

An evaluation of Offerors' past performance information will be conducted prior to any communications with Offerors leading to establishment of the competitive range. However, this evaluation will not be conducted of any Offeror whose proposal will not be admitted to the competitive range on the basis of the results of the evaluation of factors other than past performance.

The evaluation will be based on information obtained from references provided by the Offeror, other relevant past performance information obtained from other sources known to the Government, and any information supplied by the Offeror concerning problems encountered on the identified contracts and corrective action taken.

The government will assess the relative risks associated with each Offeror. Performance risks are those associated with an Offeror's likelihood of success in performing the acquisition requirements as indicated by that Offeror's record of past performance.

The assessment of performance risk is not intended to be a product of a mechanical or mathematical analysis of an Offeror's performance on a list of contracts but rather the product of subjective judgment by the Government after it considers relevant information.

When assessing performance risks, the Government will focus on the past performance of the Offeror as it relates to all acquisition requirements, such as the Offeror's record of performing according to specifications, including standards of good workmanship; the Offeror's record of controlling and forecasting costs; the Offeror's adherence to contract schedules, including the administrative aspects of performance; the Offeror's reputation for reasonable and cooperative behavior and commitment to customer satisfaction; and generally, the Offeror's business-like concern for the interest of the customer.

The Government will consider the currency and relevance of the information, source of the information, context of the data, and general trends in the Offeror's performance.

The lack of a relevant performance record may result in an unknown performance risk assessment, which will neither be used to the advantage nor disadvantage of the Offeror.

6. EXTENT OF SMALL DISADVANTAGED BUSINESS PARTICIPATION

SDB participation will not be scored, but the Government's conclusions about overall commitment and realism of the Offeror's SDB Participation targets will be used in determining the relative merits of the Offeror's proposal and in selecting the Offeror whose proposal is considered to offer the best value to the Government. The extent of the Offeror's Small Disadvantaged Business Participation Targets will be evaluated before determination of the competitive range. Evaluation of SDB participation will be assessed based on consideration of the information presented in the Offeror's proposal. The Government is seeking to determine whether the Offeror has demonstrated a commitment to use SDB concerns for the work that it intends to perform.

Offers will be evaluated on the following sub-factors:

(a) Extent of commitment to use SDB concerns
(b) Realism of the proposal
(c) Extent of participation of SDB concerns in terms of the value of the total acquisition.

APPENDIX A

PRIMATE IMMUNOLOGY AND VIROLOGY SUPPORT CONTRACTS

NIAID supports three contracts that function as central laboratories to conduct immunological and virological assays. These laboratories provide uniform evaluation of the immune responses and/or degree of efficacy elicited by vaccines and microbicides and other agents evaluated in studies conducted at the SVEUs. These contracts are:

1) **The Primate Cellular Immunology Laboratory (N01-AI30033):**

   Principal Investigator: Dr. Norman Letvin
   Institution: Beth Israel Deaconess Hospital/ Harvard Medical School, Boston, Massachusetts

   Description: This contract can conduct a variety of assays to evaluate cellular immune responses elicited in nonhuman primates by immunization or virus infection. The assays include SIV- and HIV-specific ELISPOT assays, intracellular cytokine staining (ICS) assays, flow cytometric phenotypic analysis, cytolytic (CTL) assays, tetramer assays. While most of the analysis is done using peripheral blood lymphocytes, assays using tissue biopsies are under development.

2) **The Neutralizing Antibody Assay Laboratory (N01-AI30034):**

   Principal Investigator: Dr. David Montefiori
   Institution: Duke University, Durham, North Carolina

   Description: This contract conducts assays to detect SIV, SHIV, and HIV-specific neutralizing antibodies in the serum of immunized and/or infected animals. Sera can be evaluated for the ability to neutralize the proposed challenge virus as well as a variety of virus isolates (various SHIVs, SIVs, and HIVs). Sera that can neutralize the initial set of viruses used for screening purposes can be tested against an expanding array of primary HIV-1 isolates. The laboratory conducts neutralization assays using peripheral blood lymphocytes as targets, as well as more recently developed (and more rapid) assays that use cell lines, especially reporter gene-containing cells, as targets.

3) **The Viral RNA Assay Laboratory (N01-AI30057):**

   Principal Investigator: Dr. Ranajit Pal
   Institution: Advance BioScience Laboratories, Kensington, Maryland

   Description: This contract conducts assays to detect SIV, SHIV, and HIV viral RNA in plasma and tissues of virus-infected animals. It currently uses an internally controlled, quantitative NASBA assay for most ranges of viral RNA concentration, plus a qualitative NASBA assay for detection of low level of viral RNA. A real-time quantitative NASBA assay is under development.

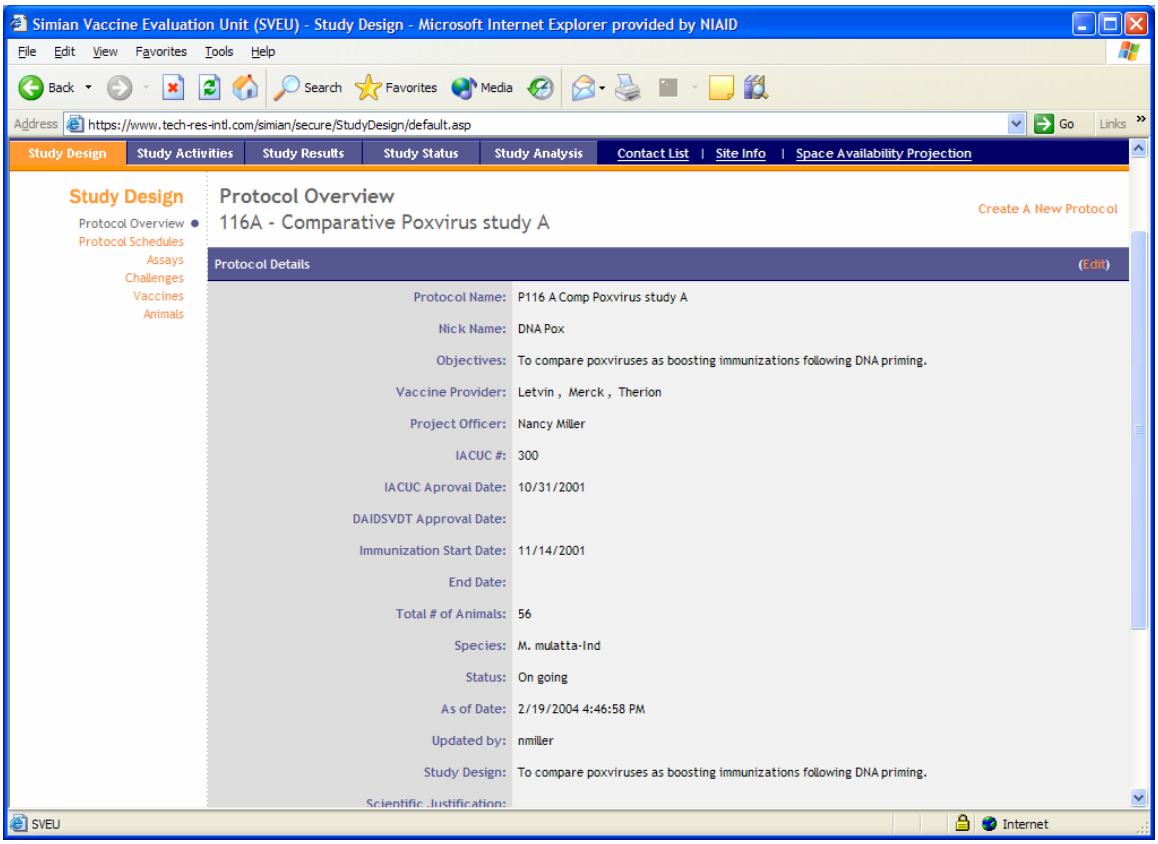
APPENDIX B:

(1) SAMPLE OF AIDS VACCINE STUDY PROTOCOL DATA INPUT FOR DAIDS SVEU DATABASE:

SAMPLE SCREENS FROM THE DAIDS SVEU DATABASE

- Study Design
  - Protocol Overview
  - Protocol Schedules
    - Protocol Groups
    - Immunization Schedule
    - Challenge Schedule
    - Sample Collection Schedule
    - Summary Schedule
- Study Information
  - List of Assays to be Performed
  - List of Challenge Virus(es)
  - List of Vaccines
  - List of Animals
- Study Activities
  - Immunizations
  - Challenge
  - Sample Collection

(2) THE ABSTRACT OF ARTICLE DESCRIBING THE STUDY


Simian Vaccine Evaluation Unit (SVEU) - Study Design - Microsoft Internet Explorer provided by NIAID
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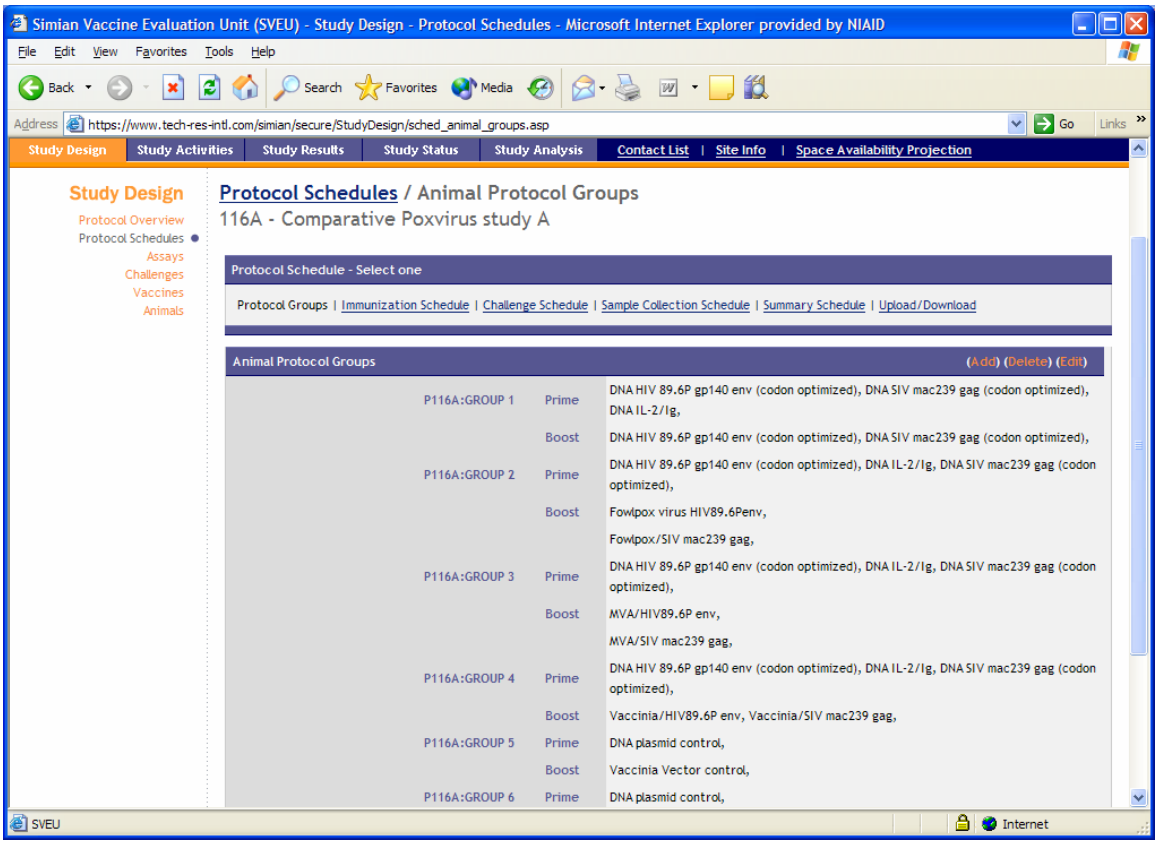
Go Links
Study Design | Study Activities | Study Results | Study Status | Study Analysis | Contact List | Site Info | Space Availability Projection
Study Design
Protocol Overview
Protocol Schedules
Assays
Challenges
Vaccines
Animals
Protocol Overview
116A - Comparative Poxvirus study A
Create A New Protocol
Protocol Details (Edit)
Protocol Name: P116 A Comp Poxvirus study A
Nick Name: DNA Pox
Objectives: To compare poxviruses as boosting immunizations following DNA priming.
Vaccine Provider: Letvin , Merck , Therion
Project Officer: Nancy Miller
IACUC #: 300
IACUC Aproval Date: 10/31/2001
DAIDSVDT Approval Date:
Immunization Start Date: 11/14/2001
End Date:
Total # of Animals: 56
Species: M. mulatta-Ind
Status: On going
As of Date: 2/19/2004 4:46:58 PM
Updated by: nmiller
Study Design: To compare poxviruses as boosting immunizations following DNA priming.
Scientific Justification:
SVEU
Internet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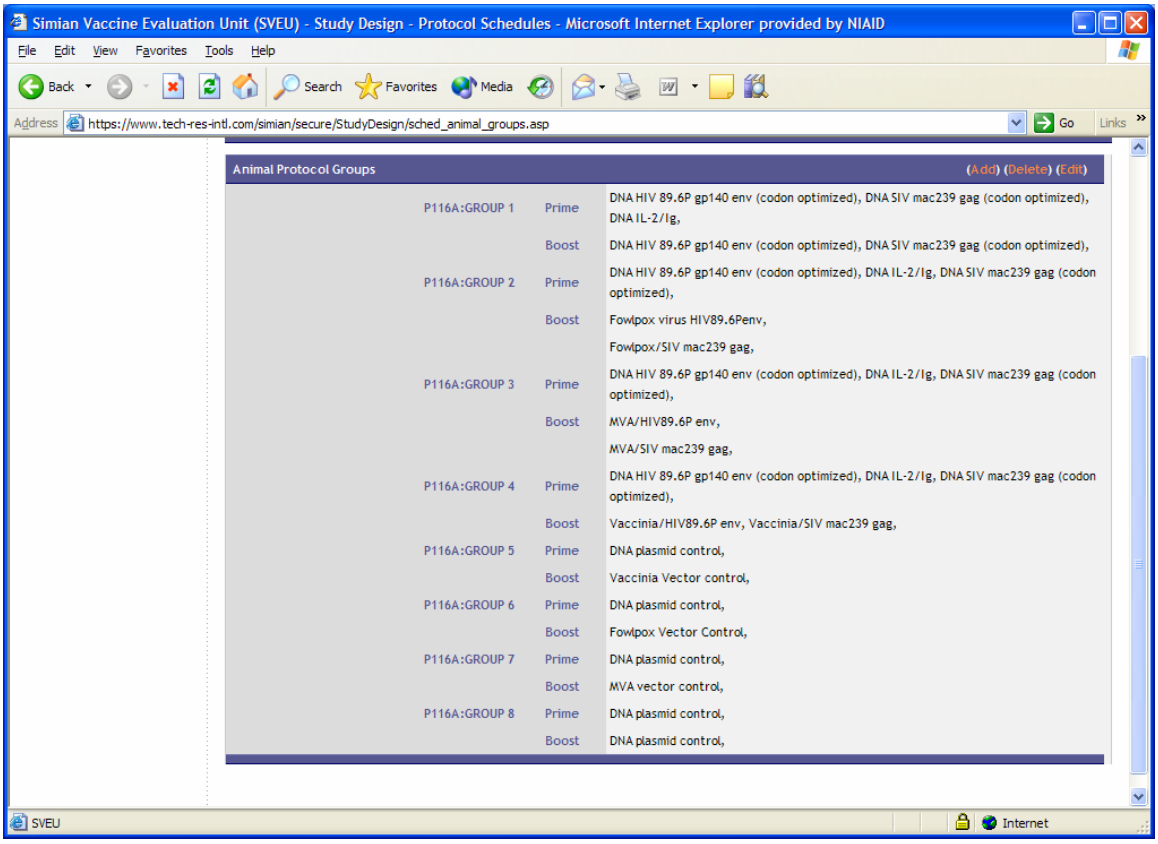
Go Links
Study Design | Study Activities | Study Results | Study Status | Study Analysis | Contact List | Site Info | Space Availability Projection
Study Design
Protocol Overview
Protocol Schedules
Assays
Challenges
Vaccines
Animals
Protocol Schedules / Animal Protocol Groups
116A - Comparative Poxvirus study A
Protocol Schedule - Select one
Protocol Groups | Immunization Schedule | Challenge Schedule | Sample Collection Schedule | Summary Schedule | Upload/Download
Animal Protocol Groups
(Add) (Delete) (Edit)
P116A:GROUP 1 Prime DNA HIV 89.6P gp140 env (codon optimized), DNA SIV mac239 gag (codon optimized), DNA IL-2/Ig,
Boost DNA HIV 89.6P gp140 env (codon optimized), DNA SIV mac239 gag (codon optimized),
P116A:GROUP 2 Prime DNA HIV 89.6P gp140 env (codon optimized), DNA IL-2/Ig, DNA SIV mac239 gag (codon optimized),
Boost Fowlpox virus HIV89.6Penv,
Fowlpox/SIV mac239 gag,
P116A:GROUP 3 Prime DNA HIV 89.6P gp140 env (codon optimized), DNA IL-2/Ig, DNA SIV mac239 gag (codon optimized),
Boost MVA/HIV89.6P env,
MVA/SIV mac239 gag,
P116A:GROUP 4 Prime DNA HIV 89.6P gp140 env (codon optimized), DNA IL-2/Ig, DNA SIV mac239 gag (codon optimized),
Boost Vaccinia/HIV89.6P env, Vaccinia/SIV mac239 gag,
P116A:GROUP 5 Prime DNA plasmid control,
Boost Vaccinia Vector control,
P116A:GROUP 6 Prime DNA plasmid control,
SVEU
Internet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Animal Protocol Groups (Add) (Delete) (Edit)
P116A:GROUP 1 Prime DNA HIV 89.6P gp140 env (codon optimized), DNA SIV mac239 gag (codon optimized), DNA IL-2/Ig,
Boost DNA HIV 89.6P gp140 env (codon optimized), DNA SIV mac239 gag (codon optimized),
P116A:GROUP 2 Prime DNA HIV 89.6P gp140 env (codon optimized), DNA IL-2/Ig, DNA SIV mac239 gag (codon optimized),
Boost Fowlpox virus HIV89.6Penv,
Fowlpox/SIV mac239 gag,
P116A:GROUP 3 Prime DNA HIV 89.6P gp140 env (codon optimized), DNA IL-2/Ig, DNA SIV mac239 gag (codon optimized),
Boost MVA/HIV89.6P env,
MVA/SIV mac239 gag,
P116A:GROUP 4 Prime DNA HIV 89.6P gp140 env (codon optimized), DNA IL-2/Ig, DNA SIV mac239 gag (codon optimized),
Boost Vaccinia/HIV89.6P env, Vaccinia/SIV mac239 gag,
P116A:GROUP 5 Prime DNA plasmid control,
Boost Vaccinia Vector control,
P116A:GROUP 6 Prime DNA plasmid control,
Boost Fowlpox Vector Control,
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Boost MVA vector control,
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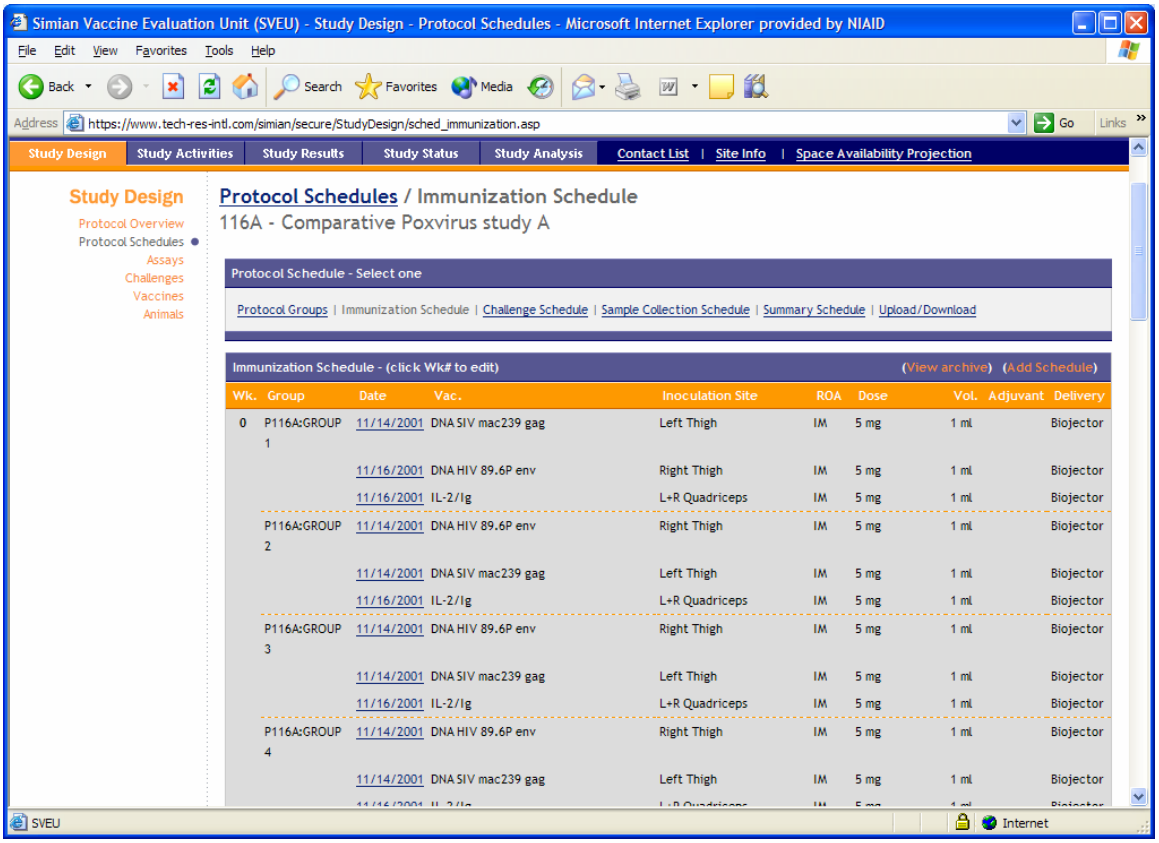
SVEU
Internet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Study Design | Study Activities | Study Results | Study Status | Study Analysis | Contact List | Site Info | Space Availability Projection
Study Design
Protocol Overview
Protocol Schedules
Assays
Challenges
Vaccines
Animals
Protocol Schedules / Immunization Schedule
116A - Comparative Poxvirus study A
Protocol Schedule - Select one
Protocol Groups | Immunization Schedule | Challenge Schedule | Sample Collection Schedule | Summary Schedule | Upload/Download
Immunization Schedule - (click Wk# to edit)
(View archive) (Add Schedule)
Wk. Group Date Vac. Inoculation Site ROA Dose Vol. Adjuvant Delivery
0 P116A:GROUP 1 11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
P116A:GROUP 2 11/14/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
P116A:GROUP 3 11/14/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
P116A:GROUP 4 11/14/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
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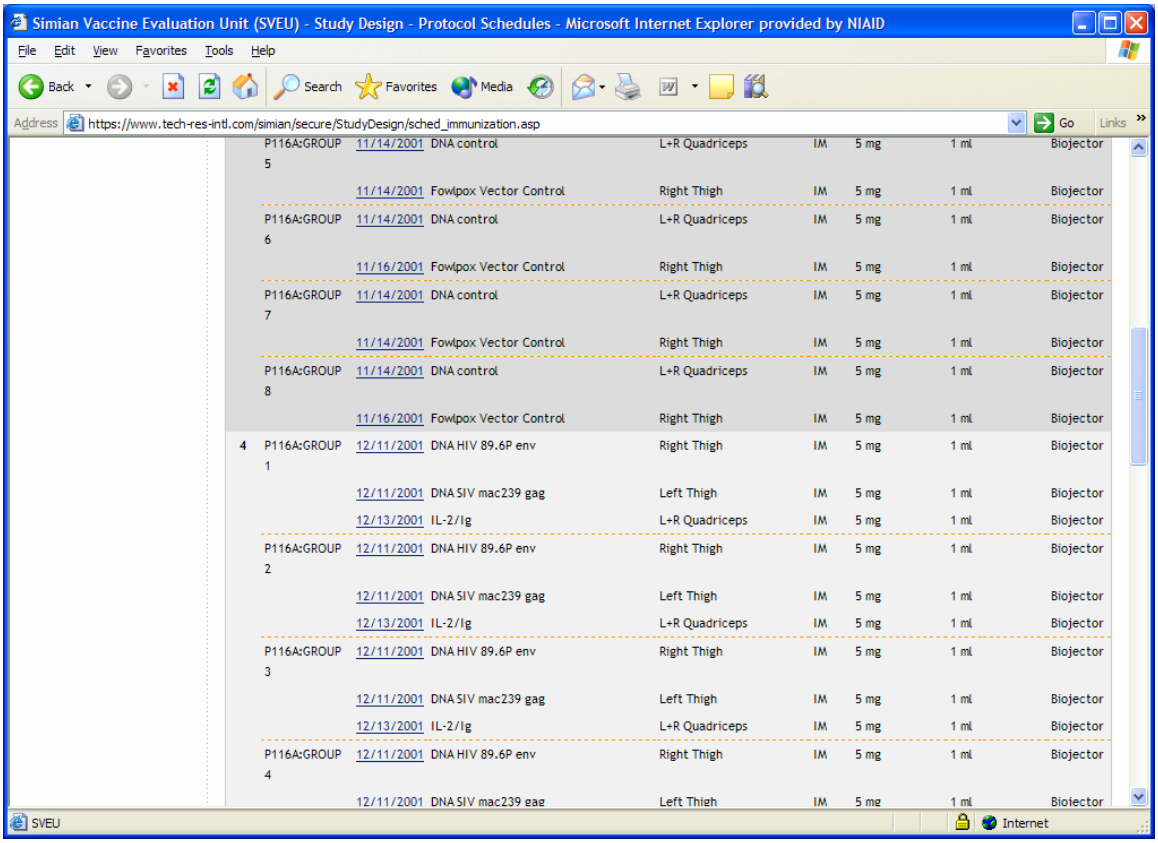
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P116A:GROUP 5 11/14/2001 DNA control L+R Quadriceps IM 5 mg 1 ml Biojector
11/14/2001 Fowlpox Vector Control Right Thigh IM 5 mg 1 ml Biojector
P116A:GROUP 6 11/14/2001 DNA control L+R Quadriceps IM 5 mg 1 ml Biojector
11/16/2001 Fowlpox Vector Control Right Thigh IM 5 mg 1 ml Biojector
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11/14/2001 Fowlpox Vector Control Right Thigh IM 5 mg 1 ml Biojector
P116A:GROUP 8 11/14/2001 DNA control L+R Quadriceps IM 5 mg 1 ml Biojector
11/16/2001 Fowlpox Vector Control Right Thigh IM 5 mg 1 ml Biojector
4 P116A:GROUP 1 12/11/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
12/11/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
12/13/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
P116A:GROUP 2 12/11/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
12/11/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
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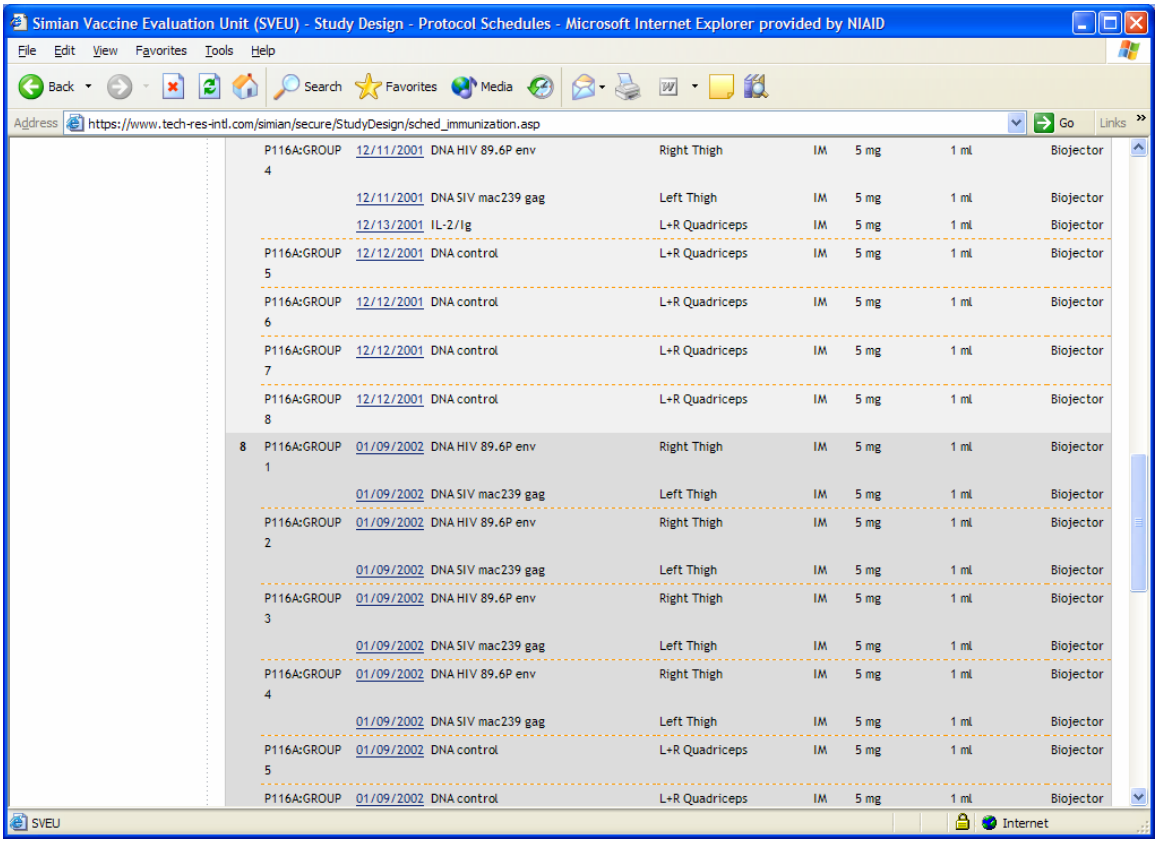
12/11/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
12/13/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
P116A:GROUP 4 12/11/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
12/11/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
SVEU
Internet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P116A:GROUP 4 12/11/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
12/11/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
12/13/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
P116A:GROUP 5 12/12/2001 DNA control L+R Quadriceps IM 5 mg 1 ml Biojector
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01/09/2002 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
P116A:GROUP 2 01/09/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
01/09/2002 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
P116A:GROUP 3 01/09/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
01/09/2002 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
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01/09/2002 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
P116A:GROUP 5 01/09/2002 DNA control L+R Quadriceps IM 5 mg 1 ml Biojector
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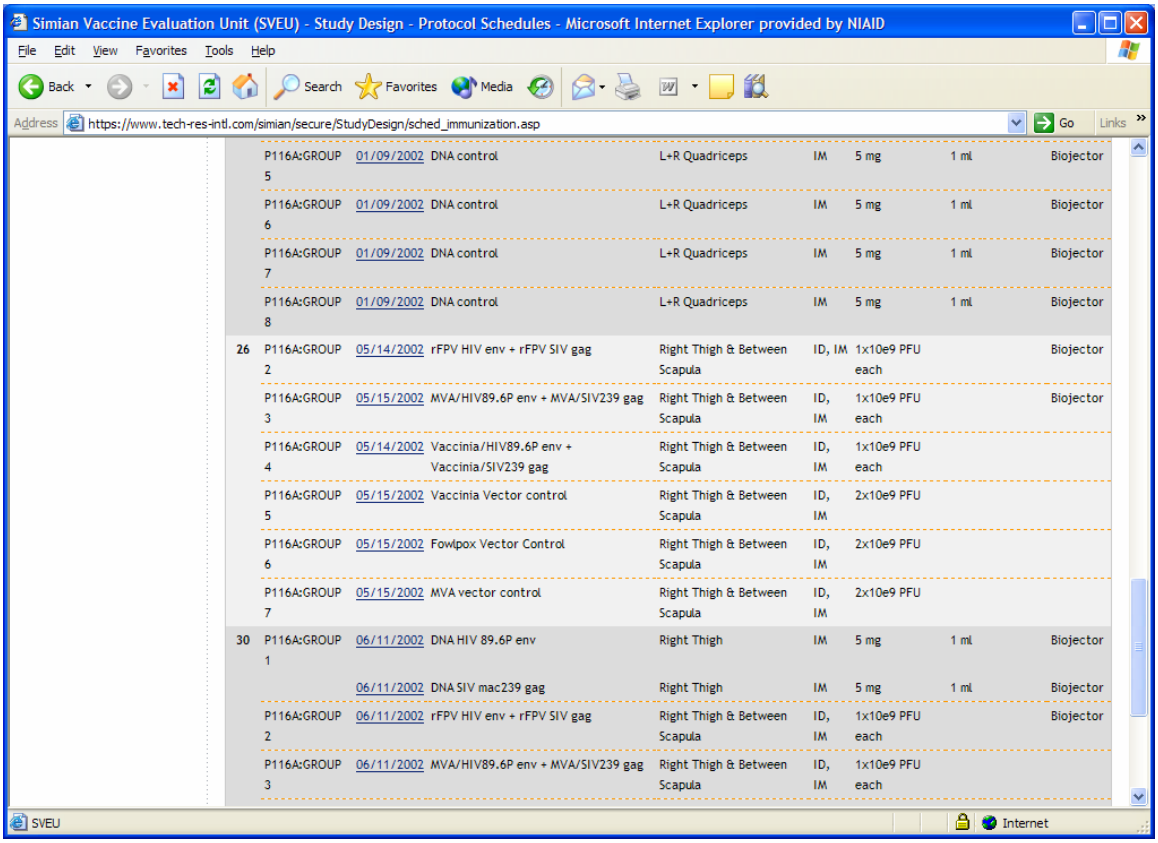
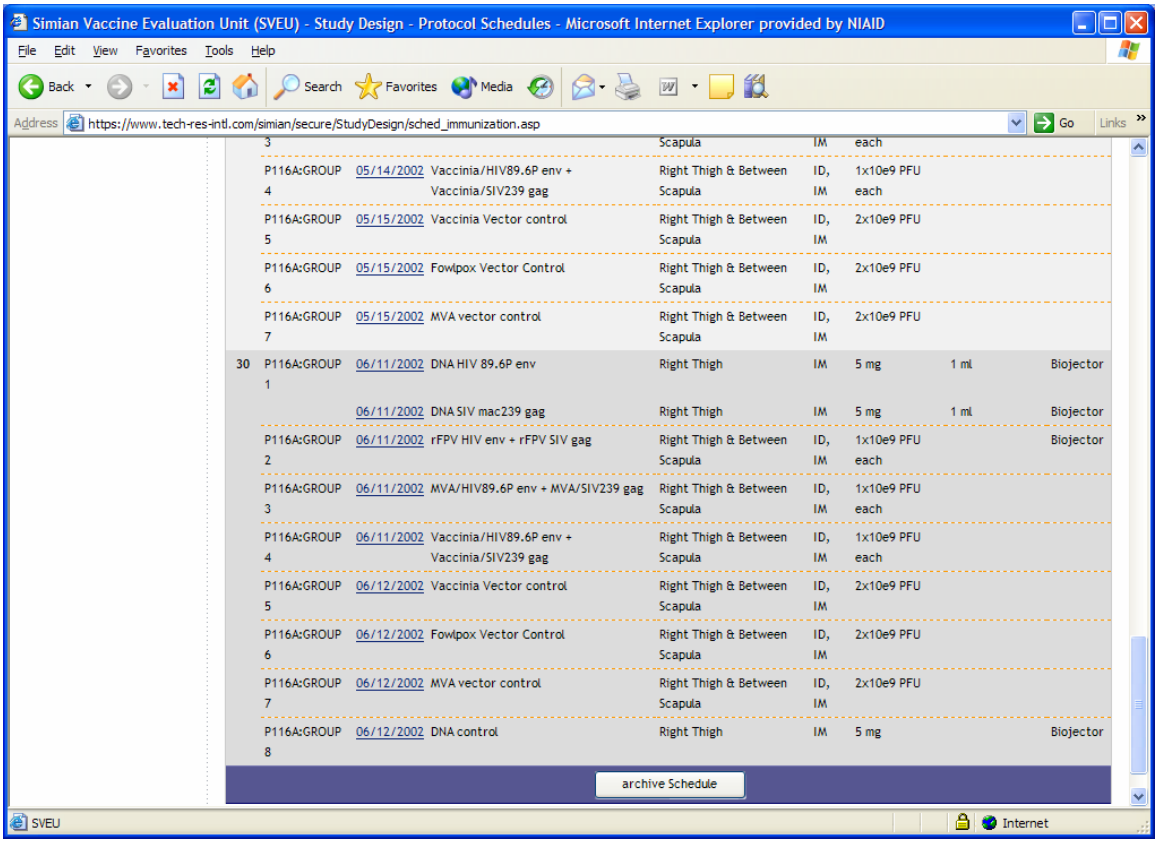


	P116A:GROUP 5	01/09/2002	DNA control	L+R Quadriceps	IM	5 mg	1 ml	Biojector
	P116A:GROUP 6	01/09/2002	DNA control	L+R Quadriceps	IM	5 mg	1 ml	Biojector
	P116A:GROUP 7	01/09/2002	DNA control	L+R Quadriceps	IM	5 mg	1 ml	Biojector
	P116A:GROUP 8	01/09/2002	DNA control	L+R Quadriceps	IM	5 mg	1 ml	Biojector
26	P116A:GROUP 2	05/14/2002	rFPV HIV env + rFPV SIV gag	Right Thigh & Between Scapula	ID, IM	1x10e9 PFU each		Biojector
	P116A:GROUP 3	05/15/2002	MVA/HIV89.6P env + MVA/SIV239 gag	Right Thigh & Between Scapula	ID, IM	1x10e9 PFU each		Biojector
	P116A:GROUP 4	05/14/2002	Vaccinia/HIV89.6P env + Vaccinia/SIV239 gag	Right Thigh & Between Scapula	ID, IM	1x10e9 PFU each		
	P116A:GROUP 5	05/15/2002	Vaccinia Vector control	Right Thigh & Between Scapula	ID, IM	2x10e9 PFU		
	P116A:GROUP 6	05/15/2002	Fowlpox Vector Control	Right Thigh & Between Scapula	ID, IM	2x10e9 PFU		
	P116A:GROUP 7	05/15/2002	MVA vector control	Right Thigh & Between Scapula	ID, IM	2x10e9 PFU		
30	P116A:GROUP 1	06/11/2002	DNA HIV 89.6P env	Right Thigh	IM	5 mg	1 ml	Biojector
		06/11/2002	DNA SIV mac239 gag	Right Thigh	IM	5 mg	1 ml	Biojector
	P116A:GROUP 2	06/11/2002	rFPV HIV env + rFPV SIV gag	Right Thigh & Between Scapula	ID, IM	1x10e9 PFU each		Biojector
	P116A:GROUP 3	06/11/2002	MVA/HIV89.6P env + MVA/SIV239 gag	Right Thigh & Between Scapula	ID, IM	1x10e9 PFU each		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3 Scapula IM each
P116A:GROUP 4 05/14/2002 Vaccinia/HIV89.6P env + Vaccinia/SIV239 gag Right Thigh & Between Scapula ID, IM 1x10e9 PFU each
P116A:GROUP 5 05/15/2002 Vaccinia Vector control Right Thigh & Between Scapula ID, IM 2x10e9 PFU
P116A:GROUP 6 05/15/2002 Fowlpox Vector Control Right Thigh & Between Scapula ID, IM 2x10e9 PFU
P116A:GROUP 7 05/15/2002 MVA vector control Right Thigh & Between Scapula ID, IM 2x10e9 PFU
30 P116A:GROUP 1 06/11/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
06/11/2002 DNA SIV mac239 gag Right Thigh IM 5 mg 1 ml Biojector
P116A:GROUP 2 06/11/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x10e9 PFU each Biojector
P116A:GROUP 3 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x10e9 PFU each
P116A:GROUP 4 06/11/2002 Vaccinia/HIV89.6P env + Vaccinia/SIV239 gag Right Thigh & Between Scapula ID, IM 1x10e9 PFU each
P116A:GROUP 5 06/12/2002 Vaccinia Vector control Right Thigh & Between Scapula ID, IM 2x10e9 PFU
P116A:GROUP 6 06/12/2002 Fowlpox Vector Control Right Thigh & Between Scapula ID, IM 2x10e9 PFU
P116A:GROUP 7 06/12/2002 MVA vector control Right Thigh & Between Scapula ID, IM 2x10e9 PFU
P116A:GROUP 8 06/12/2002 DNA control Right Thigh IM 5 mg Biojector
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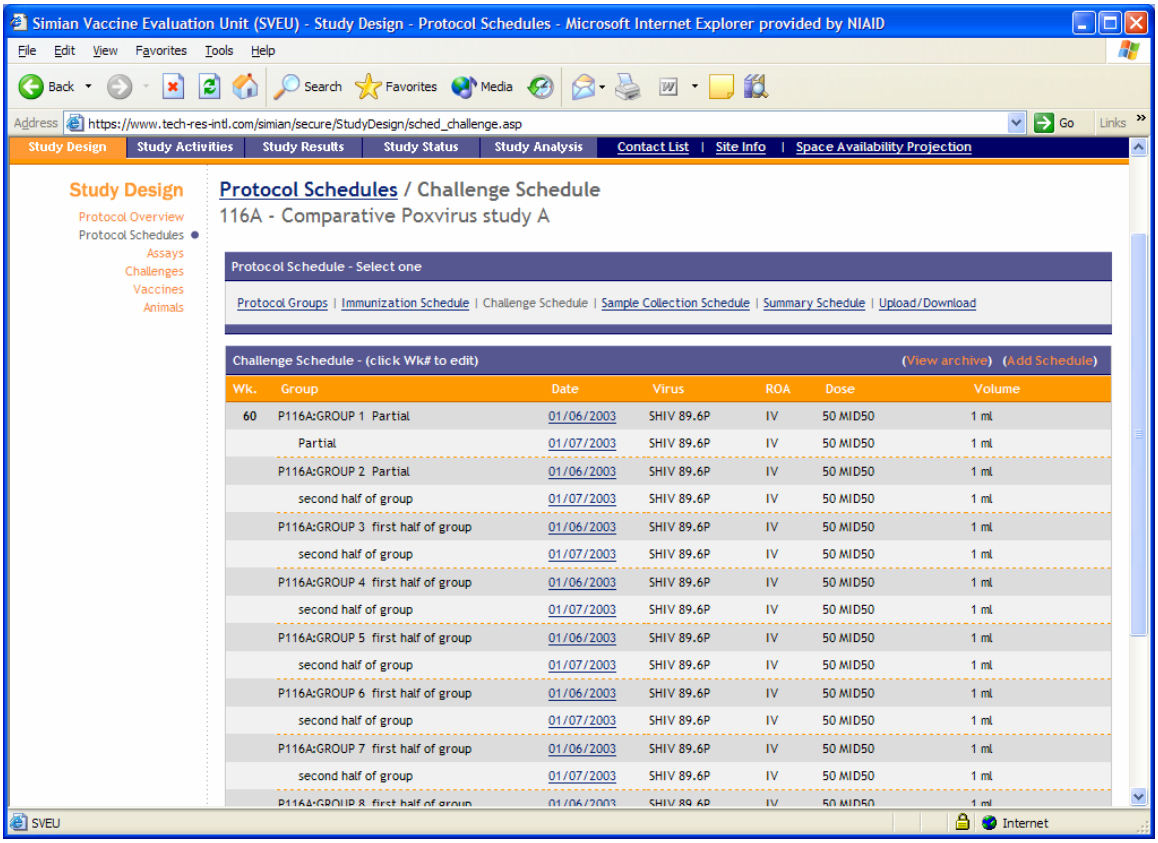
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Challenge Schedule - (click Wk# to edit)
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Wk. Group Date Virus ROA Dose Volume
60 P116A:GROUP 1 Partial 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
Partial 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
P116A:GROUP 2 Partial 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
second half of group 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
P116A:GROUP 3 first half of group 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
second half of group 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
P116A:GROUP 4 first half of group 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
second half of group 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
P116A:GROUP 5 first half of group 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
second half of group 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
P116A:GROUP 6 first half of group 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
second half of group 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
P116A:GROUP 7 first half of group 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
second half of group 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
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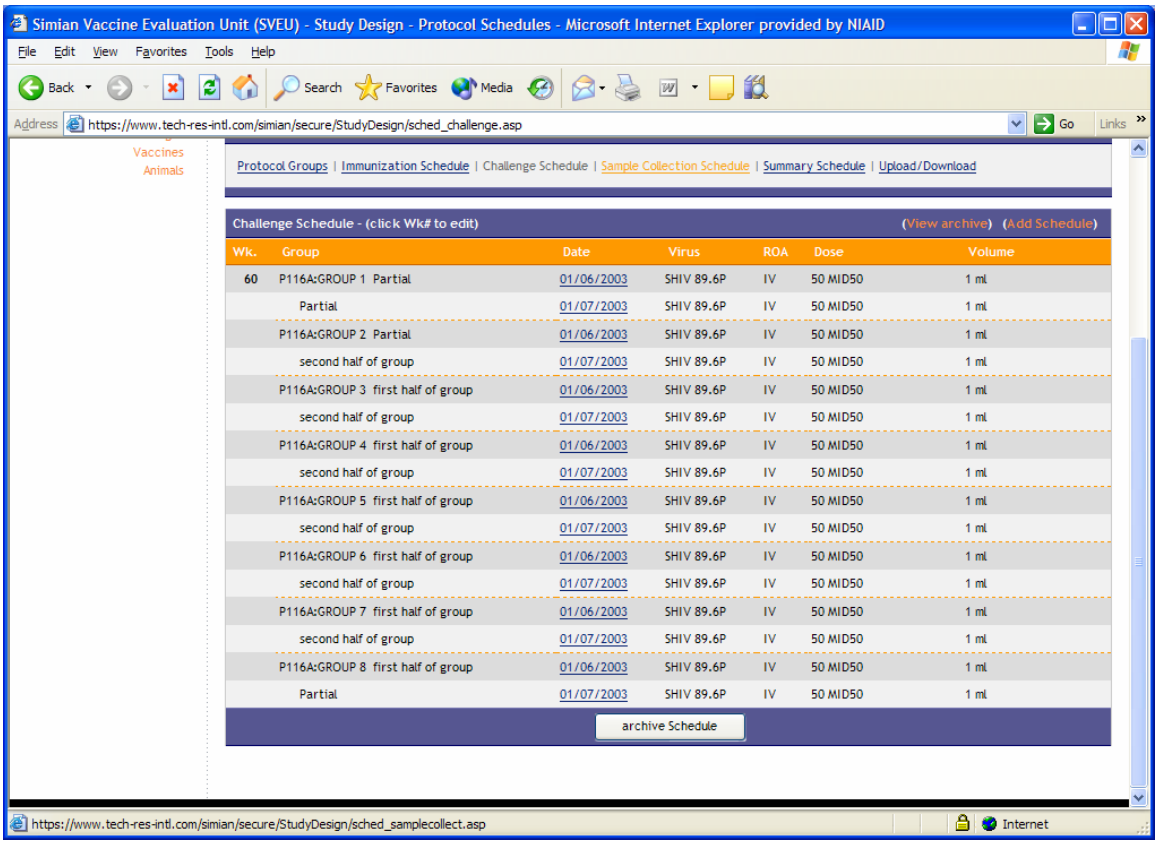
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Challenge Schedule - (click Wk# to edit)
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Wk. Group Date Virus ROA Dose Volume
60 P116A:GROUP 1 Partial 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
Partial 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
P116A:GROUP 2 Partial 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
second half of group 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
P116A:GROUP 3 first half of group 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
second half of group 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
P116A:GROUP 4 first half of group 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
second half of group 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
P116A:GROUP 5 first half of group 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
second half of group 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
P116A:GROUP 6 first half of group 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
second half of group 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
P116A:GROUP 7 first half of group 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
second half of group 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
P116A:GROUP 8 first half of group 01/06/2003 SHIV 89.6P IV 50 MID50 1 ml
Partial 01/07/2003 SHIV 89.6P IV 50 MID50 1 ml
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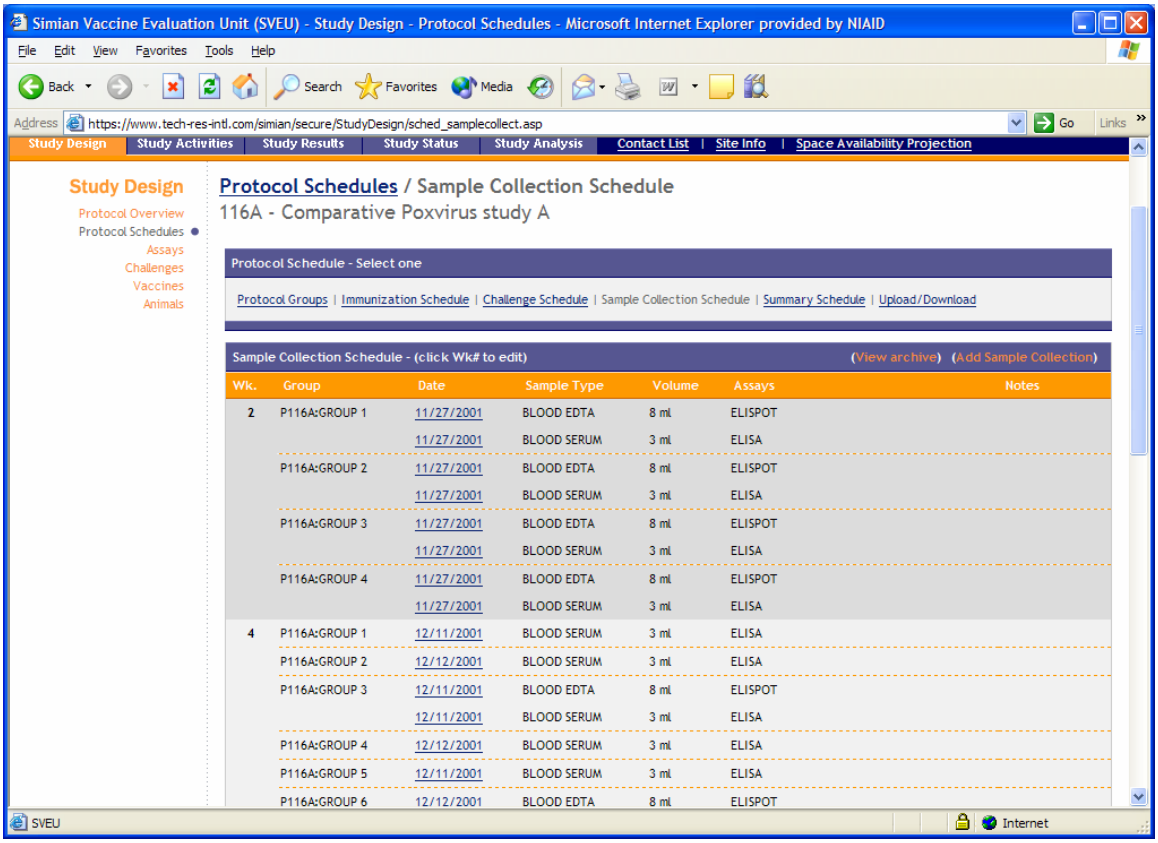
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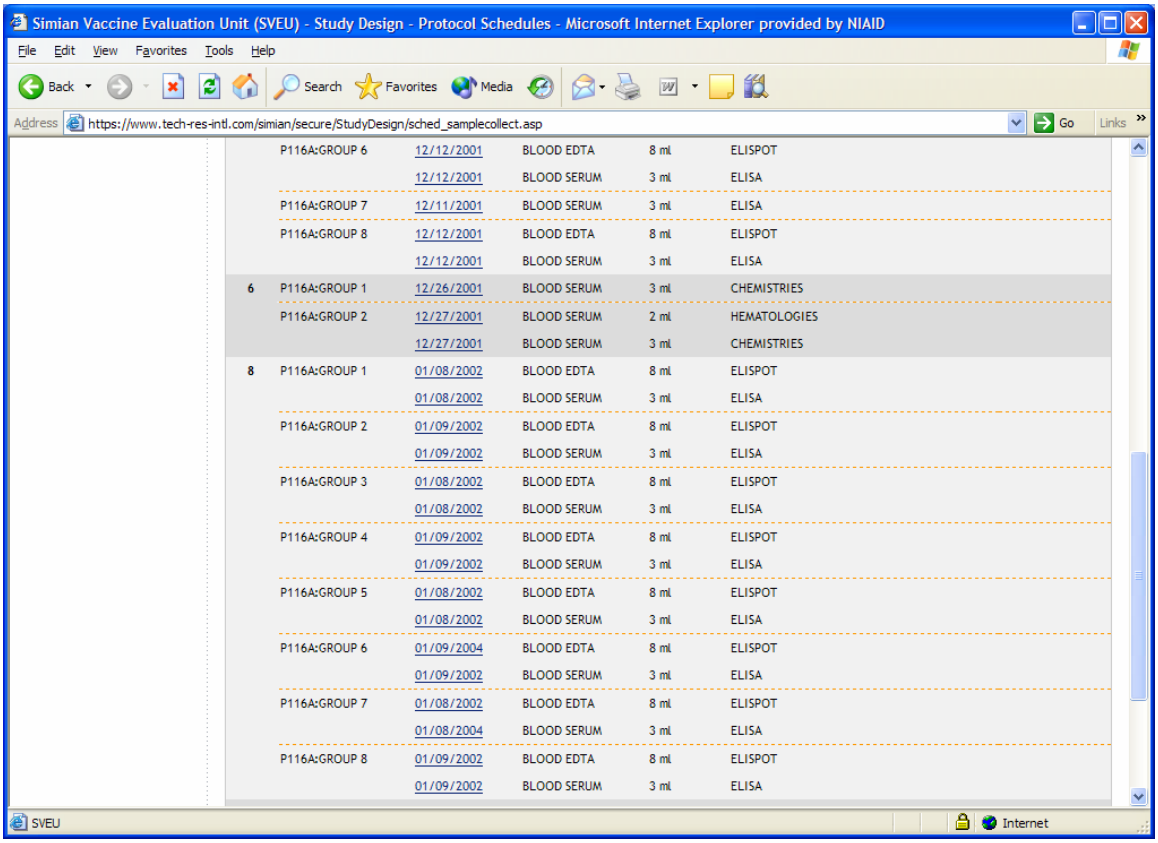
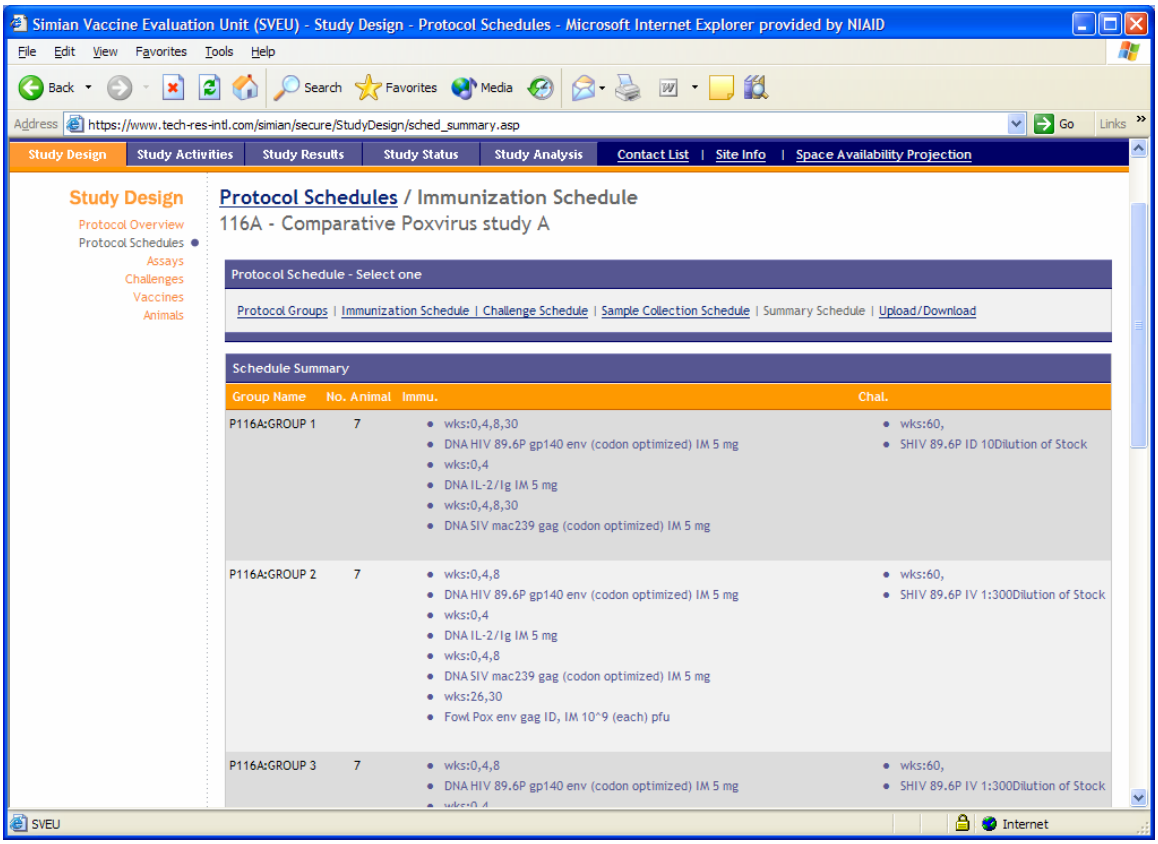
Sample Collection Schedule - (click Wk# to edit)
(View archive) (Add Sample Collection)
Wk. Group Date Sample Type Volume Assays Notes
2 P116A:GROUP 1 11/27/2001 BLOOD EDTA 8 ml ELISPOT
11/27/2001 BLOOD SERUM 3 ml ELISA
P116A:GROUP 2 11/27/2001 BLOOD EDTA 8 ml ELISPOT
11/27/2001 BLOOD SERUM 3 ml ELISA
P116A:GROUP 3 11/27/2001 BLOOD EDTA 8 ml ELISPOT
11/27/2001 BLOOD SERUM 3 ml ELISA
P116A:GROUP 4 11/27/2001 BLOOD EDTA 8 ml ELISPOT
11/27/2001 BLOOD SERUM 3 ml ELISA
4 P116A:GROUP 1 12/11/2001 BLOOD SERUM 3 ml ELISA
P116A:GROUP 2 12/12/2001 BLOOD SERUM 3 ml ELISA
P116A:GROUP 3 12/11/2001 BLOOD EDTA 8 ml ELISPOT
12/11/2001 BLOOD SERUM 3 ml ELISA
P116A:GROUP 4 12/12/2001 BLOOD SERUM 3 ml ELISA
P116A:GROUP 5 12/11/2001 BLOOD SERUM 3 ml ELISA
P116A:GROUP 6 12/12/2001 BLOOD EDTA 8 ml ELISPOT
SVEU
Internet



	P116A:GROUP 6	12/12/2001	BLOOD EDTA	8 ml	ELISPOT
		12/12/2001	BLOOD SERUM	3 ml	ELISA
	P116A:GROUP 7	12/11/2001	BLOOD SERUM	3 ml	ELISA
	P116A:GROUP 8	12/12/2001	BLOOD EDTA	8 ml	ELISPOT
		12/12/2001	BLOOD SERUM	3 ml	ELISA
6	P116A:GROUP 1	12/26/2001	BLOOD SERUM	3 ml	CHEMISTRIES
	P116A:GROUP 2	12/27/2001	BLOOD SERUM	2 ml	HEMATOLOGIES
		12/27/2001	BLOOD SERUM	3 ml	CHEMISTRIES
8	P116A:GROUP 1	01/08/2002	BLOOD EDTA	8 ml	ELISPOT
		01/08/2002	BLOOD SERUM	3 ml	ELISA
	P116A:GROUP 2	01/09/2002	BLOOD EDTA	8 ml	ELISPOT
		01/09/2002	BLOOD SERUM	3 ml	ELISA
	P116A:GROUP 3	01/08/2002	BLOOD EDTA	8 ml	ELISPOT
		01/08/2002	BLOOD SERUM	3 ml	ELISA
	P116A:GROUP 4	01/09/2002	BLOOD EDTA	8 ml	ELISPOT
		01/09/2002	BLOOD SERUM	3 ml	ELISA
	P116A:GROUP 5	01/08/2002	BLOOD EDTA	8 ml	ELISPOT
		01/08/2002	BLOOD SERUM	3 ml	ELISA
	P116A:GROUP 6	01/09/2004	BLOOD EDTA	8 ml	ELISPOT
		01/09/2002	BLOOD SERUM	3 ml	ELISA
	P116A:GROUP 7	01/08/2002	BLOOD EDTA	8 ml	ELISPOT
		01/08/2004	BLOOD SERUM	3 ml	ELISA
	P116A:GROUP 8	01/09/2002	BLOOD EDTA	8 ml	ELISPOT
		01/09/2002	BLOOD SERUM	3 ml	ELISA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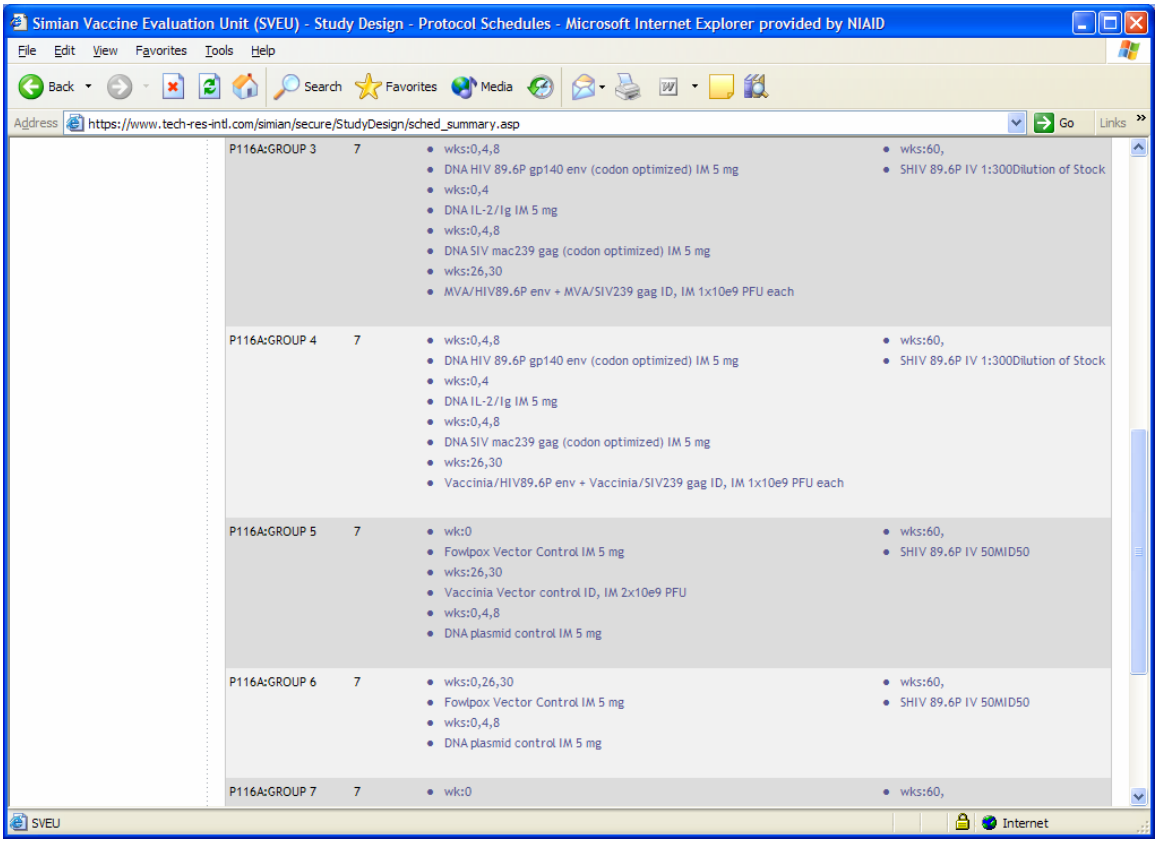
Schedule Summary
Group Name
No. Animal
Immu.
Chal.
P116A:GROUP 1
7
wks:0,4,8,30
DNA HIV 89.6P gp140 env (codon optimized) IM 5 mg
wks:0,4
DNA IL-2/Ig IM 5 mg
wks:0,4,8,30
DNA SIV mac239 gag (codon optimized) IM 5 mg
wks:60,
SHIV 89.6P ID 10Dilution of Stock
P116A:GROUP 2
7
wks:0,4,8
DNA HIV 89.6P gp140 env (codon optimized) IM 5 mg
wks:0,4
DNA IL-2/Ig IM 5 mg
wks:0,4,8
DNA SIV mac239 gag (codon optimized) IM 5 mg
wks:26,30
Fowl Pox env gag ID, IM 10^9 (each) pfu
wks:60,
SHIV 89.6P IV 1:300Dilution of Stock
P116A:GROUP 3
7
wks:0,4,8
DNA HIV 89.6P gp140 env (codon optimized) IM 5 mg
wks:60,
SHIV 89.6P IV 1:300Dilution of Stock
SVEU
Internet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P116A:GROUP 3 7
wks:0,4,8
DNA HIV 89.6P gp140 env (codon optimized) IM 5 mg
wks:0,4
DNA IL-2/Ig IM 5 mg
wks:0,4,8
DNA SIV mac239 gag (codon optimized) IM 5 mg
wks:26,30
MVA/HIV89.6P env + MVA/SIV239 gag ID, IM 1x10e9 PFU each
wks:60,
SHIV 89.6P IV 1:300Dilution of Stock
P116A:GROUP 4 7
wks:0,4,8
DNA HIV 89.6P gp140 env (codon optimized) IM 5 mg
wks:0,4
DNA IL-2/Ig IM 5 mg
wks:0,4,8
DNA SIV mac239 gag (codon optimized) IM 5 mg
wks:26,30
Vaccinia/HIV89.6P env + Vaccinia/SIV239 gag ID, IM 1x10e9 PFU each
wks:60,
SHIV 89.6P IV 1:300Dilution of Stock
P116A:GROUP 5 7
wk:0
Fowlpox Vector Control IM 5 mg
wks:26,30
Vaccinia Vector control ID, IM 2x10e9 PFU
wks:0,4,8
DNA plasmid control IM 5 mg
wks:60,
SHIV 89.6P IV 50MID50
P116A:GROUP 6 7
wks:0,26,30
Fowlpox Vector Control IM 5 mg
wks:0,4,8
DNA plasmid control IM 5 mg
wks:60,
SHIV 89.6P IV 50MID50
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wk:0
wks:60,
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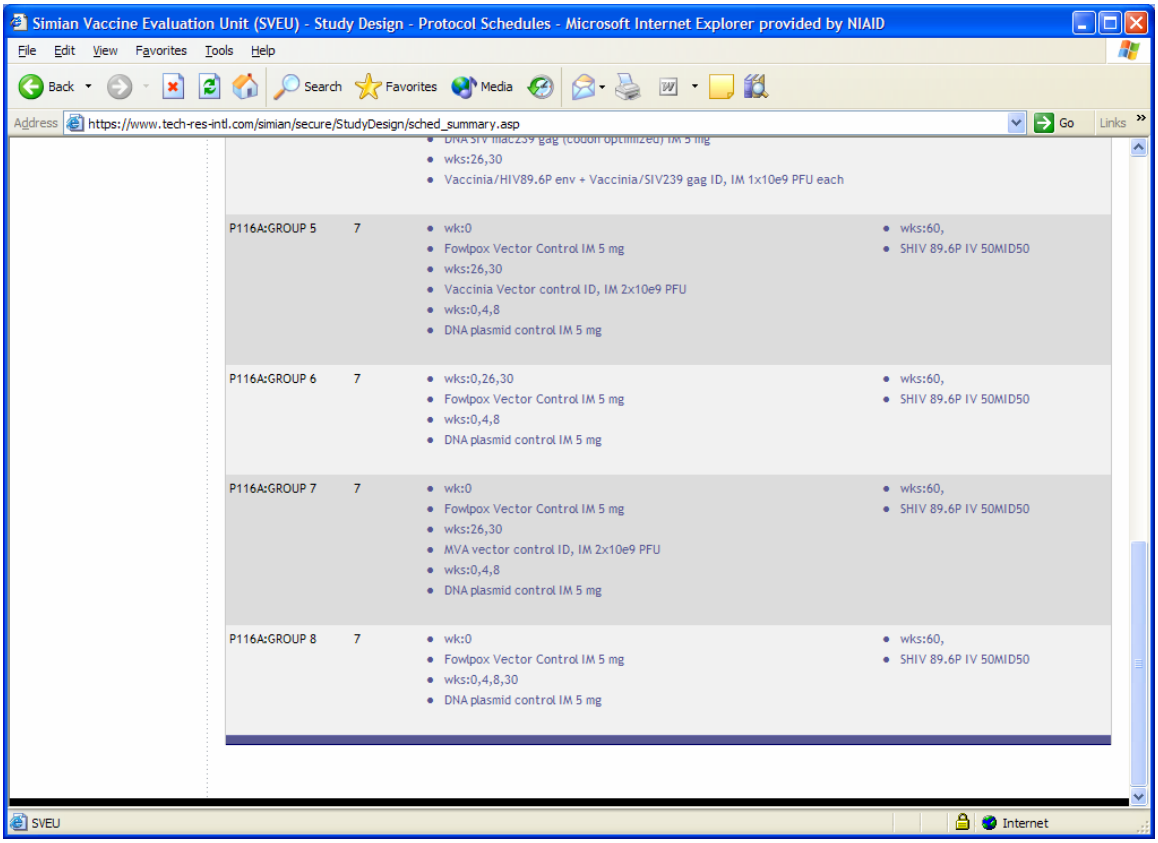
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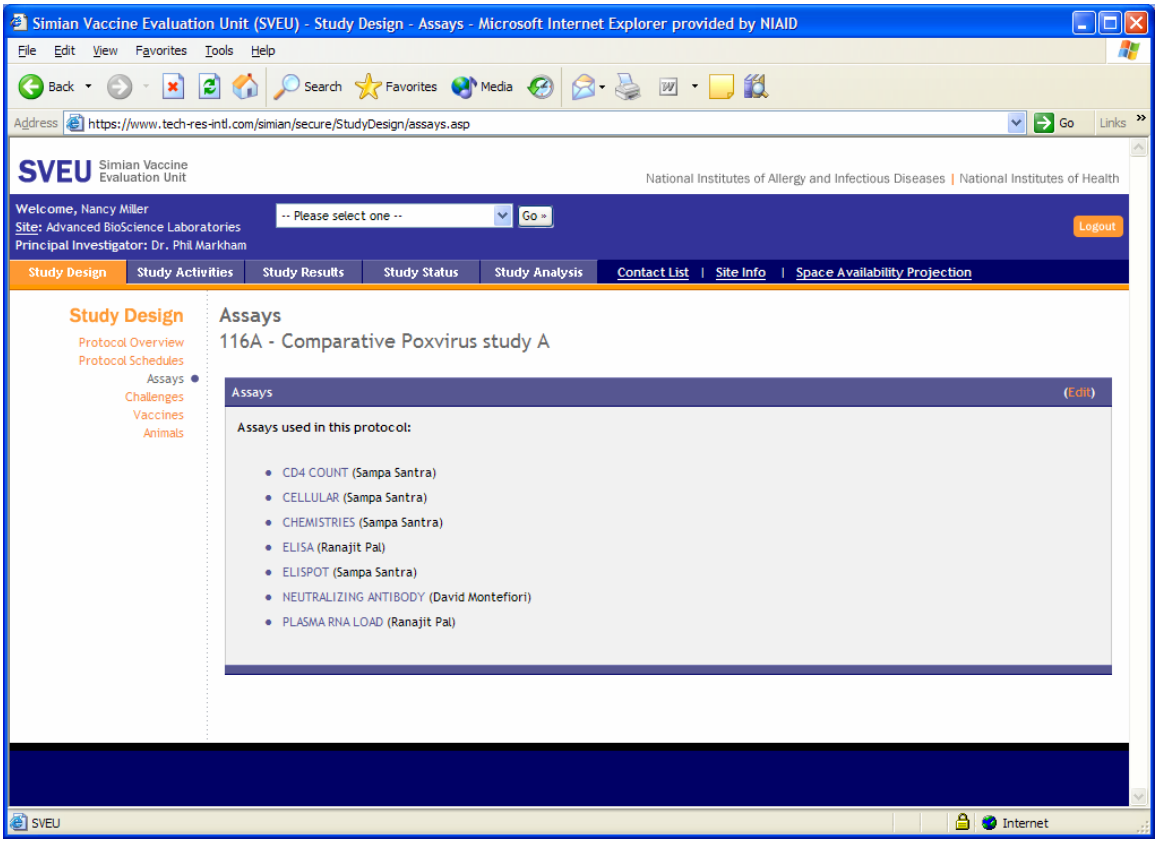
wks:26,30
Vaccinia/HIV89.6P env + Vaccinia/SIV239 gag ID, IM 1x10e9 PFU each
P116A:GROUP 5 7
wk:0
Fowlpox Vector Control IM 5 mg
wks:26,30
Vaccinia Vector control ID, IM 2x10e9 PFU
wks:0,4,8
DNA plasmid control IM 5 mg
wks:60,
SHIV 89.6P IV 50MID50
P116A:GROUP 6 7
wks:0,26,30
Fowlpox Vector Control IM 5 mg
wks:0,4,8
DNA plasmid control IM 5 mg
wks:60,
SHIV 89.6P IV 50MID50
P116A:GROUP 7 7
wk:0
Fowlpox Vector Control IM 5 mg
wks:26,30
MVA vector control ID, IM 2x10e9 PFU
wks:0,4,8
DNA plasmid control IM 5 mg
wks:60,
SHIV 89.6P IV 50MID50
P116A:GROUP 8 7
wk:0
Fowlpox Vector Control IM 5 mg
wks:0,4,8,30
DNA plasmid control IM 5 mg
wks:60,
SHIV 89.6P IV 50MID50
SVEU
Internet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Assays used in this protocol:
CD4 COUNT (Sampa Santra)
CELLULAR (Sampa Santra)
CHEMISTRIES (Sampa Santra)
ELISA (Ranajit Pal)
ELISPOT (Sampa Santra)
NEUTRALIZING ANTIBODY (David Montefiori)
PLASMA RNA LOAD (Ranajit Pal)
SVEU
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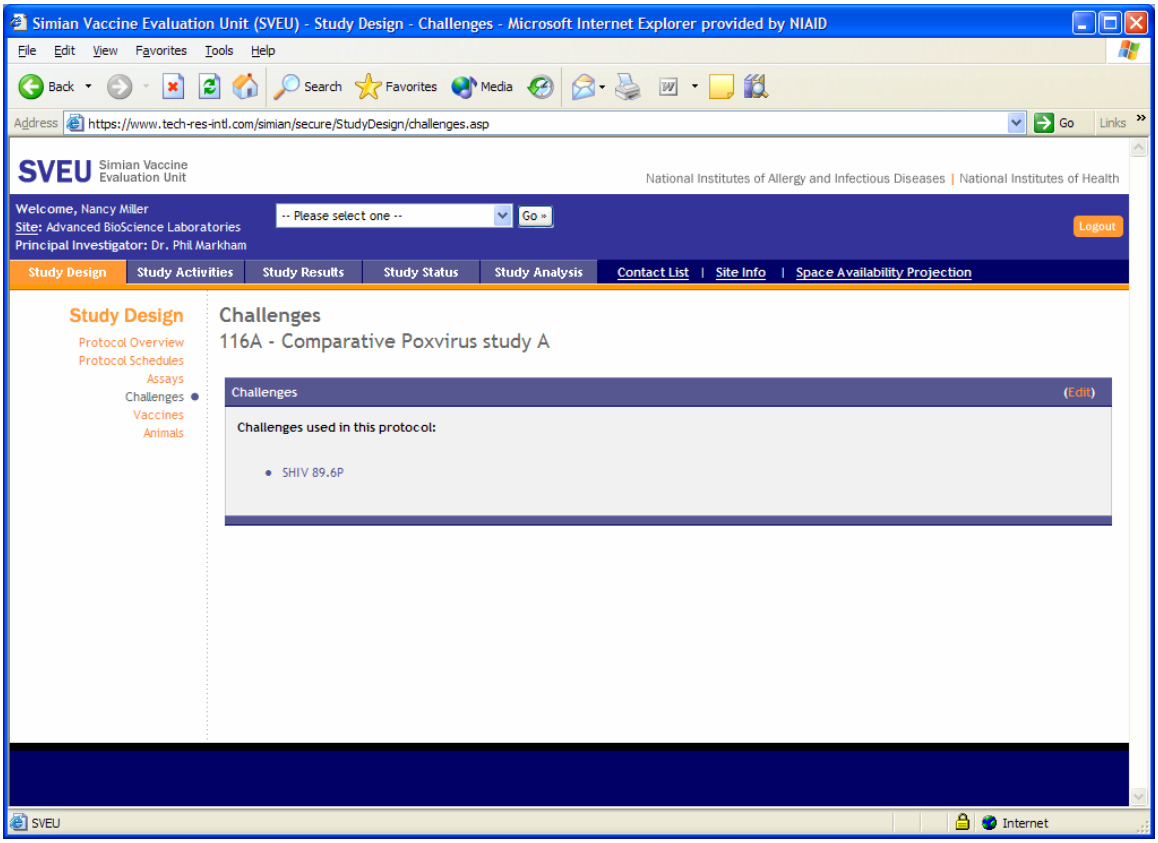
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Challenges used in this protocol:
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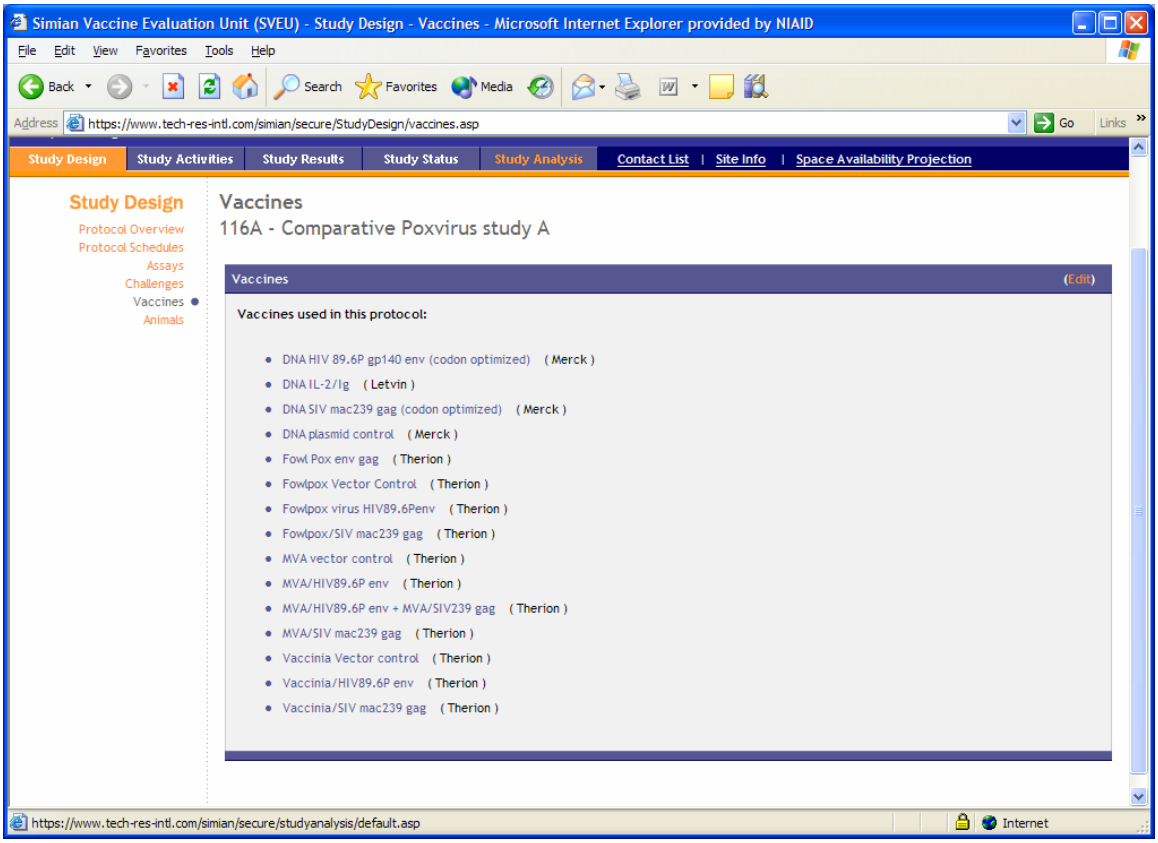
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Vaccines (Edit)
Vaccines used in this protocol:
DNA HIV 89.6P gp140 env (codon optimized) (Merck)
DNA IL-2/Ig (Letvin)
DNA SIV mac239 gag (codon optimized) (Merck)
DNA plasmid control (Merck)
Fowl Pox env gag (Therion)
Fowlpox Vector Control (Therion)
Fowlpox virus HIV89.6Penv (Therion)
Fowlpox/SIV mac239 gag (Therion)
MVA vector control (Therion)
MVA/HIV89.6P env (Therion)
MVA/HIV89.6P env + MVA/SIV239 gag (Therion)
MVA/SIV mac239 gag (Therion)
Vaccinia Vector control (Therion)
Vaccinia/HIV89.6P env (Therion)
Vaccinia/SIV mac239 gag (Therion)
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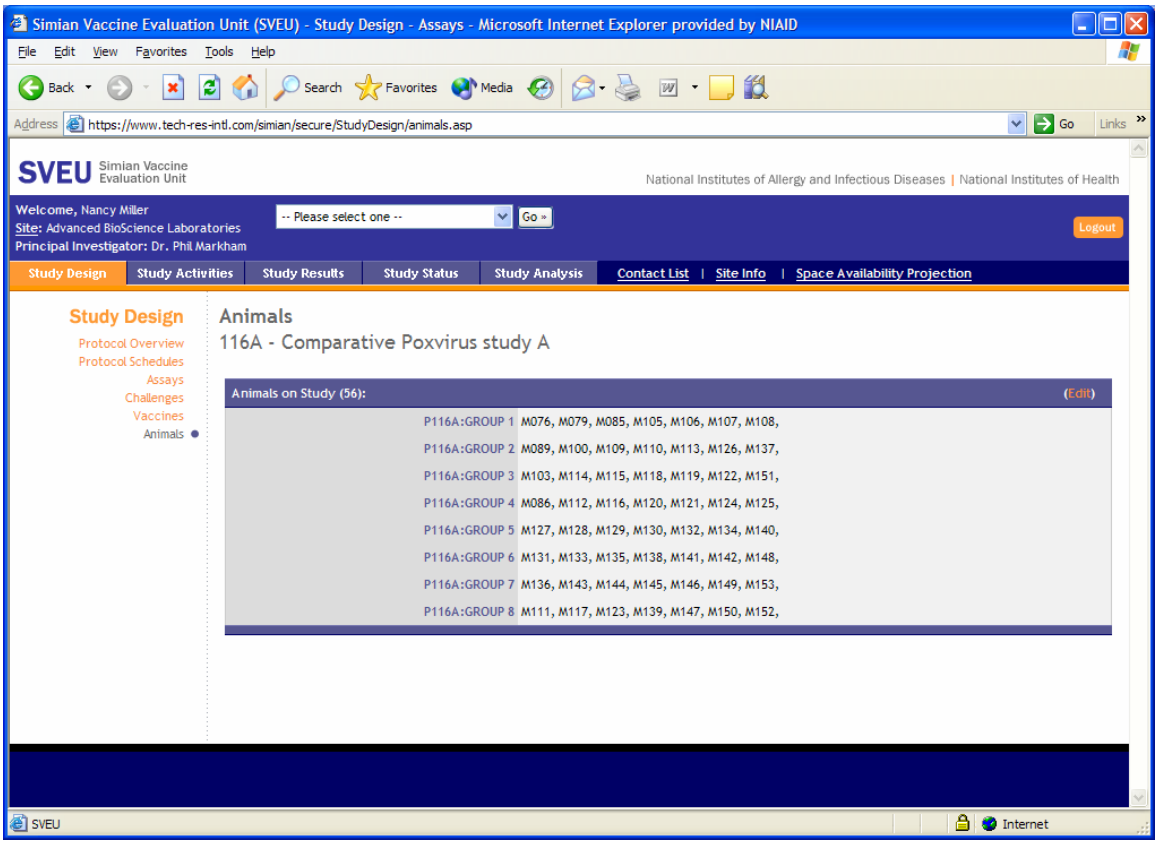
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P116A:GROUP 2 M089, M100, M109, M110, M113, M126, M137,
P116A:GROUP 3 M103, M114, M115, M118, M119, M122, M151,
P116A:GROUP 4 M086, M112, M116, M120, M121, M124, M125,
P116A:GROUP 5 M127, M128, M129, M130, M132, M134, M140,
P116A:GROUP 6 M131, M133, M135, M138, M141, M142, M148,
P116A:GROUP 7 M136, M143, M144, M145, M146, M149, M153,
P116A:GROUP 8 M111, M117, M123, M139, M147, M150, M152,
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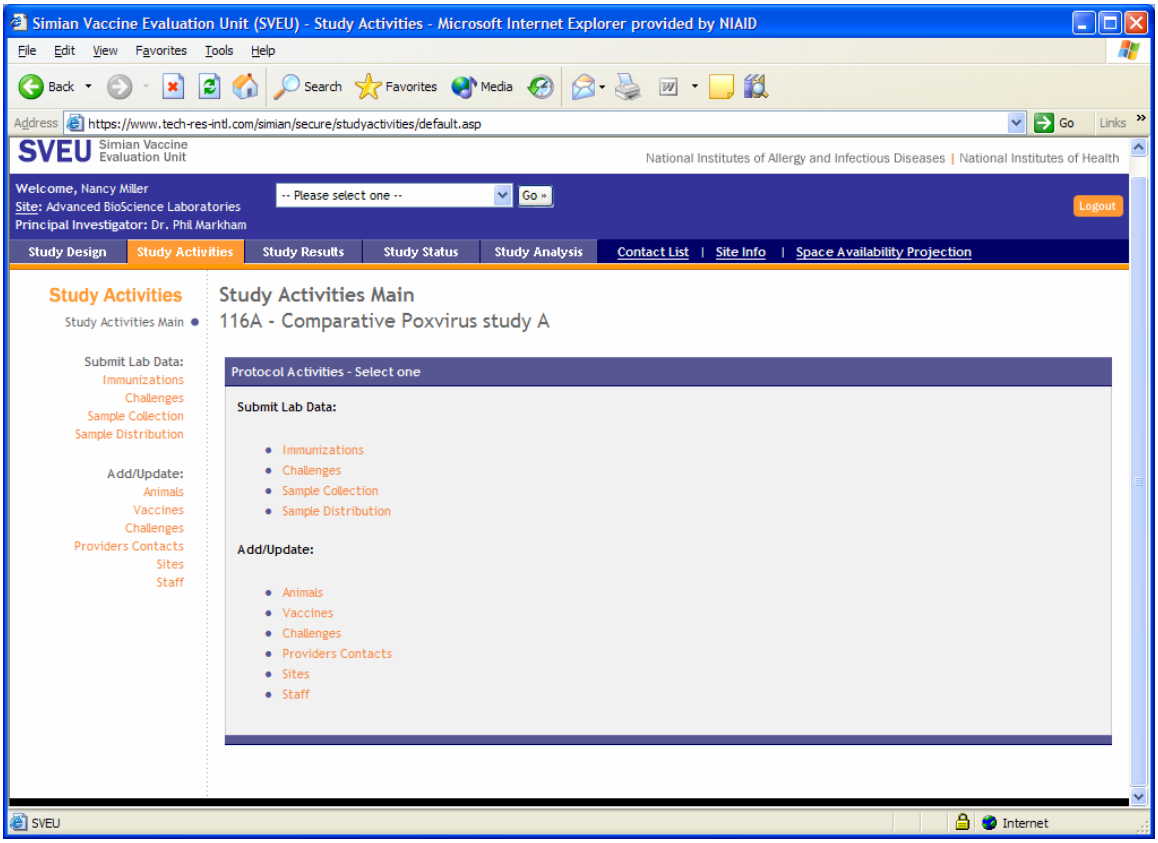
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Principal Investigator: Dr. Phil Markham
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Challenges
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Sample Distribution
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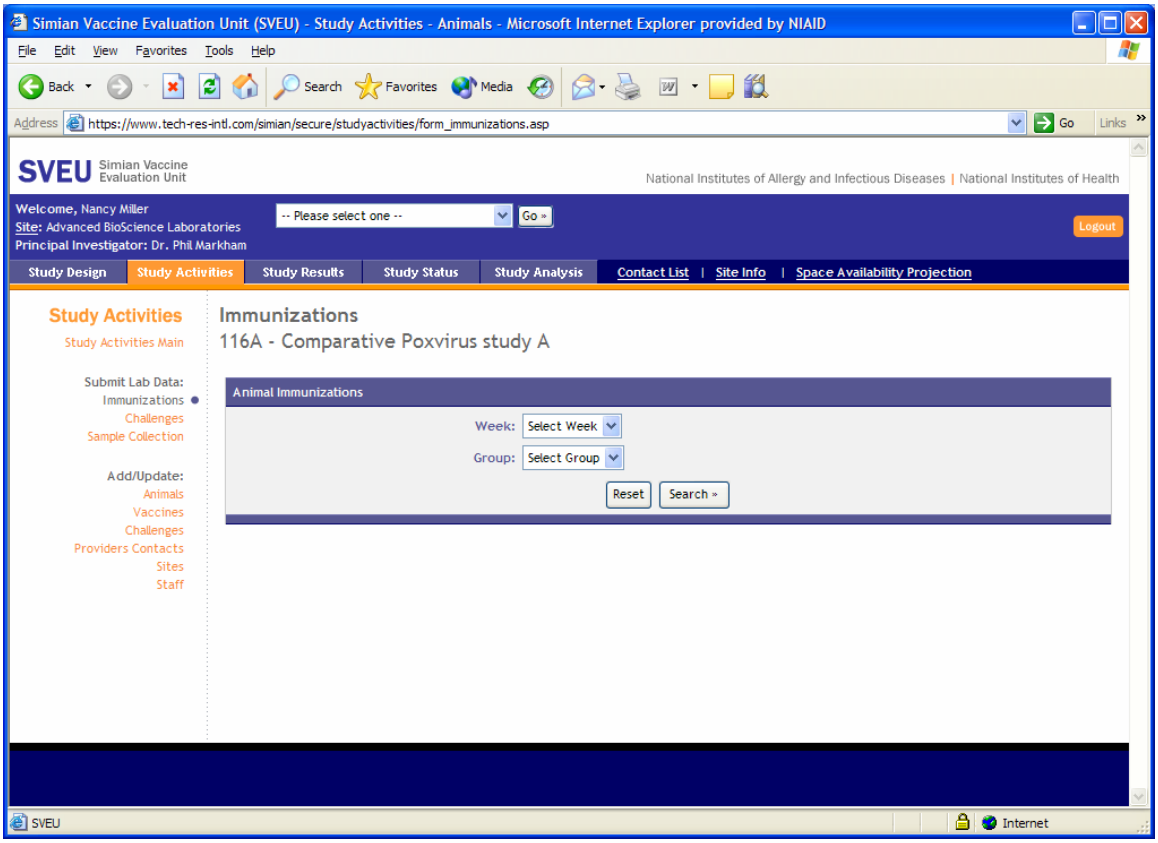
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Immunizations
116A - Comparative Poxvirus study A
Animal Immunizations
Week: Select Week
Group: Select Group
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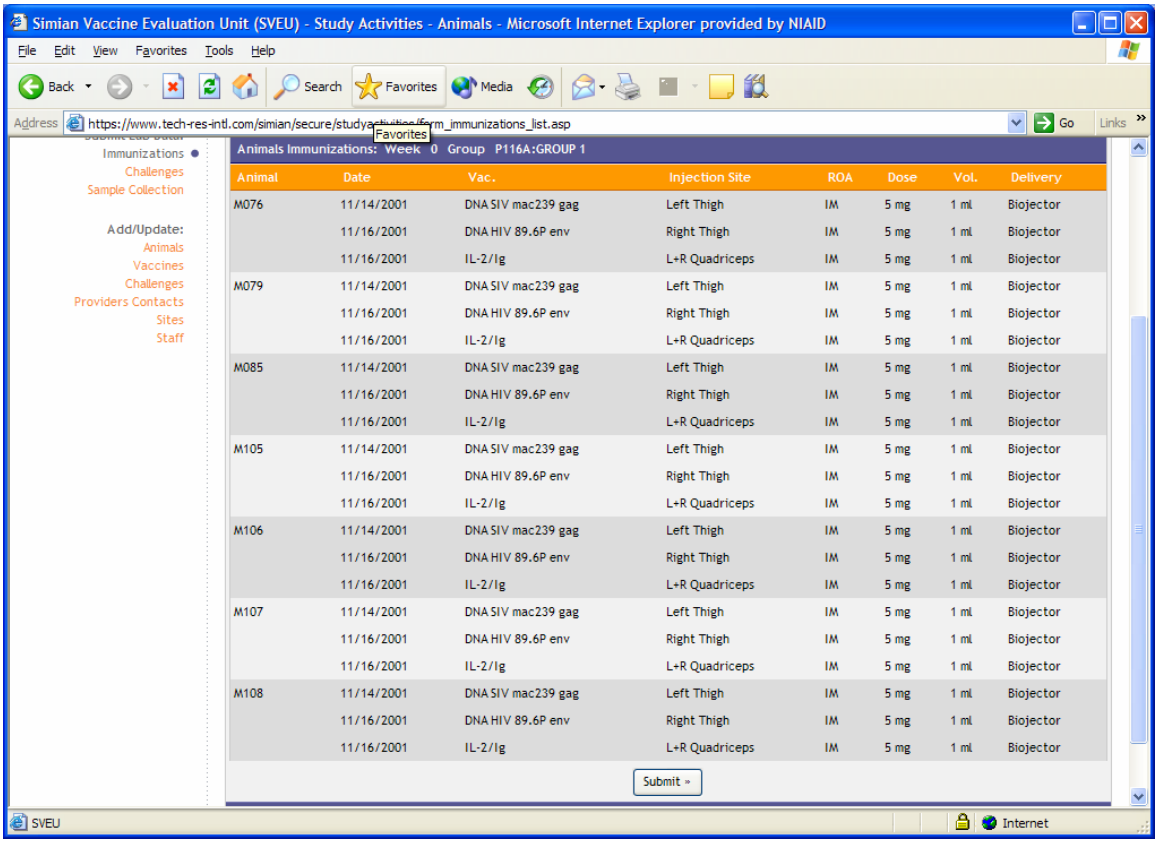
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Challenges
Sample Collection
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Animals
Vaccines
Challenges
Providers Contacts
Sites
Staff
Animals Immunizations: Week 0 Group P116A:GROUP 1
Animal Date Vac. Injection Site ROA Dose Vol. Delivery
M076 11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
M079 11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
M085 11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
M105 11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
M106 11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
M107 11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
M108 11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
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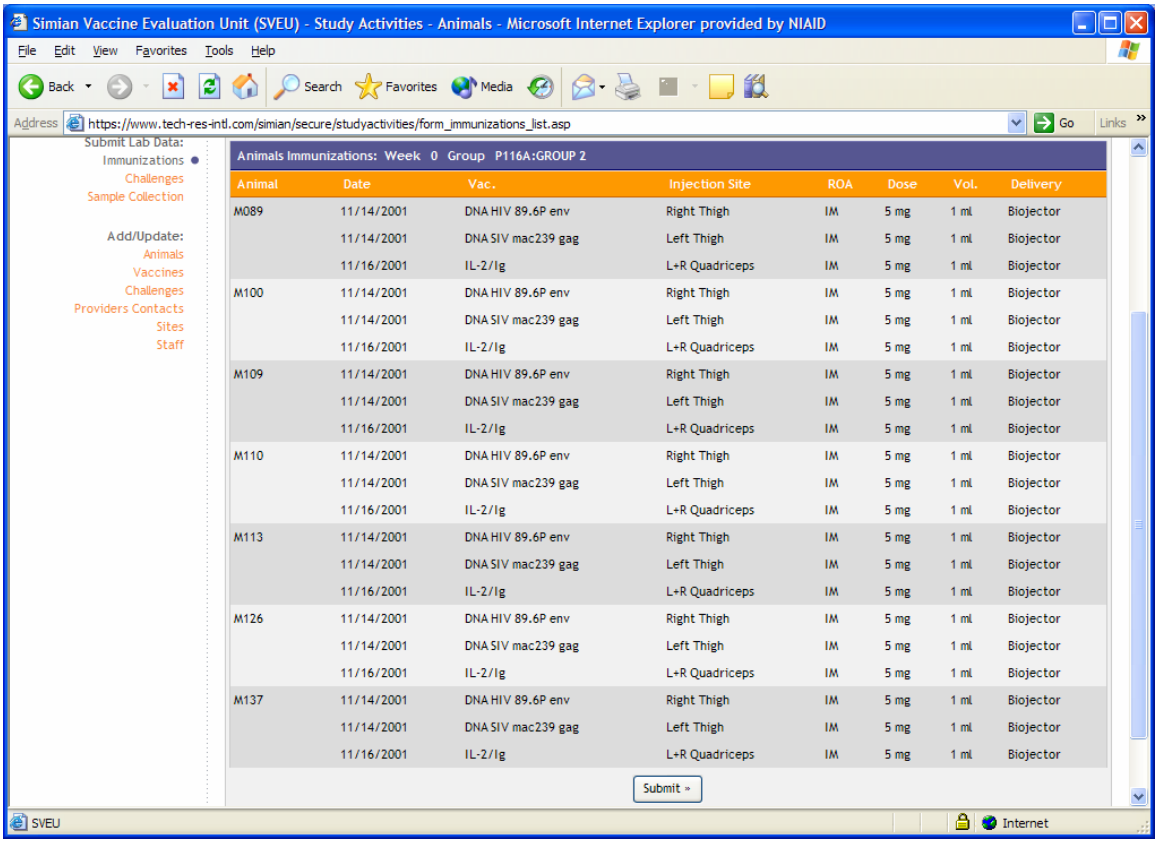
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Challenges
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Animals
Vaccines
Challenges
Providers Contacts
Sites
Staff
Animals Immunizations: Week 0 Group P116A:GROUP 2
Animal Date Vac. Injection Site ROA Dose Vol. Delivery
M089 11/14/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
M100 11/14/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
M109 11/14/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
M110 11/14/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
M113 11/14/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
M126 11/14/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
M137 11/14/2001 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
11/14/2001 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
11/16/2001 IL-2/Ig L+R Quadriceps IM 5 mg 1 ml Biojector
Submit »
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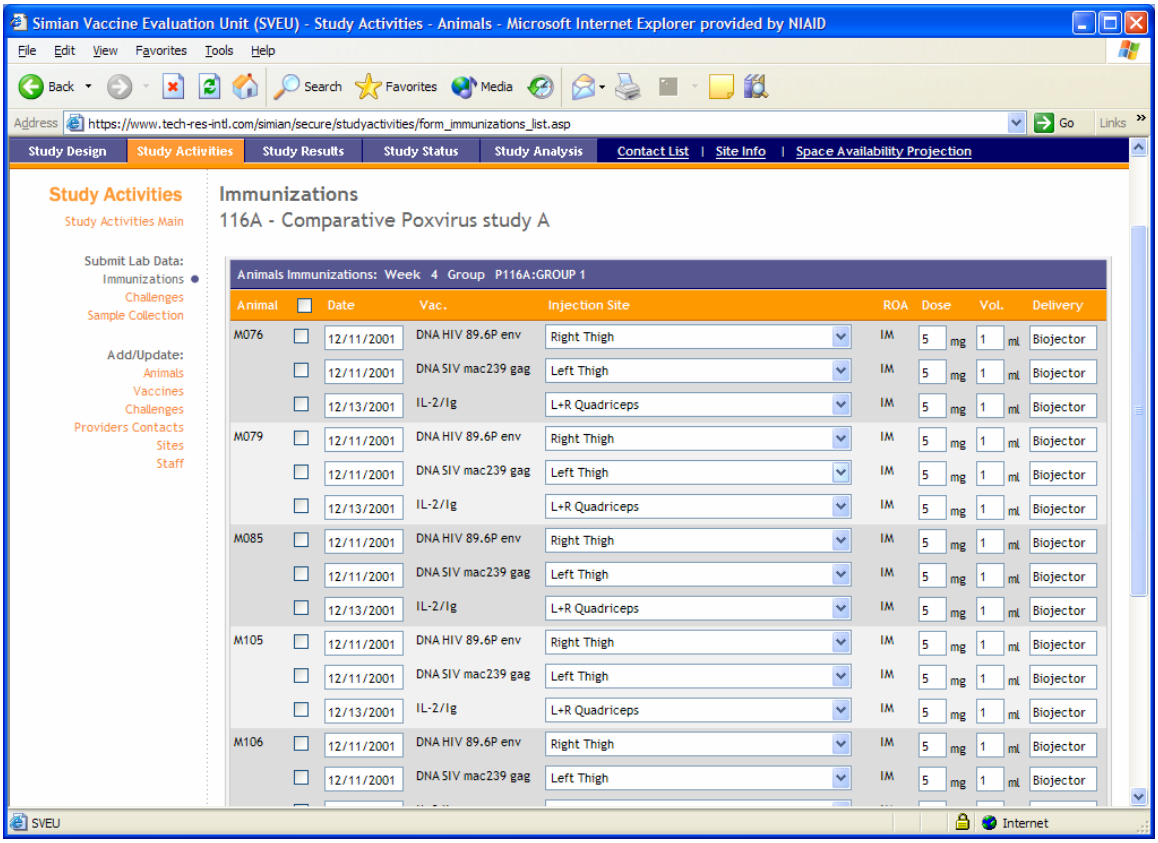
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Study Activities
Study Activities Main
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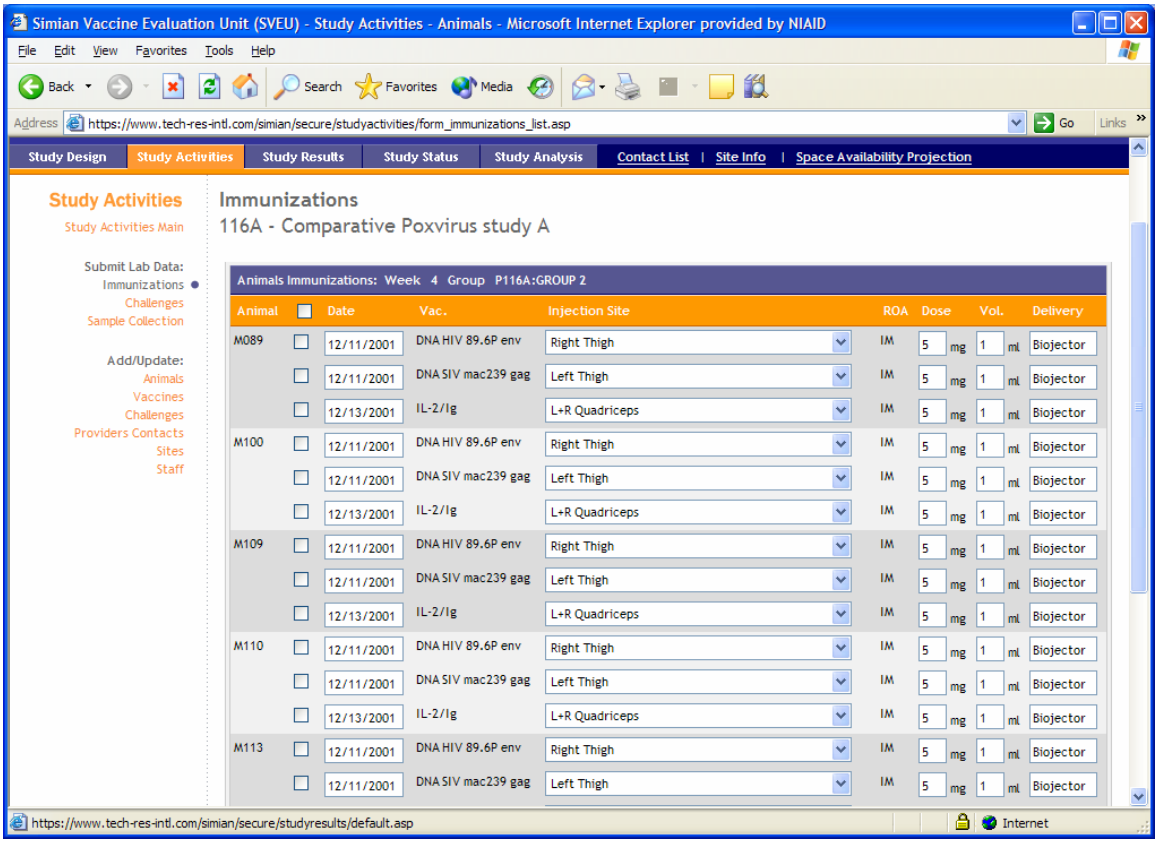
Immunizations
Challenges
Sample Collection
Add/Update:
Animals
Vaccines
Challenges
Providers Contacts
Sites
Staff
Immunizations
116A - Comparative Poxvirus study A
Animals Immunizations: Week 4 Group P116A:GROUP 1
Animal | Date | Vac. | Injection Site | ROA | Dose | Vol. | Delivery
M076 | 12/11/2001 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
12/11/2001 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
12/13/2001 | IL-2/Ig | L+R Quadriceps | IM | 5 mg | 1 ml | Biojector
M079 | 12/11/2001 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
12/11/2001 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
12/13/2001 | IL-2/Ig | L+R Quadriceps | IM | 5 mg | 1 ml | Biojector
M085 | 12/11/2001 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
12/11/2001 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
12/13/2001 | IL-2/Ig | L+R Quadriceps | IM | 5 mg | 1 ml | Biojector
M105 | 12/11/2001 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
12/11/2001 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
12/13/2001 | IL-2/Ig | L+R Quadriceps | IM | 5 mg | 1 ml | Biojector
M106 | 12/11/2001 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
12/11/2001 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
SVEU
Internet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Study Activities
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Submit Lab Data:
Immunizations
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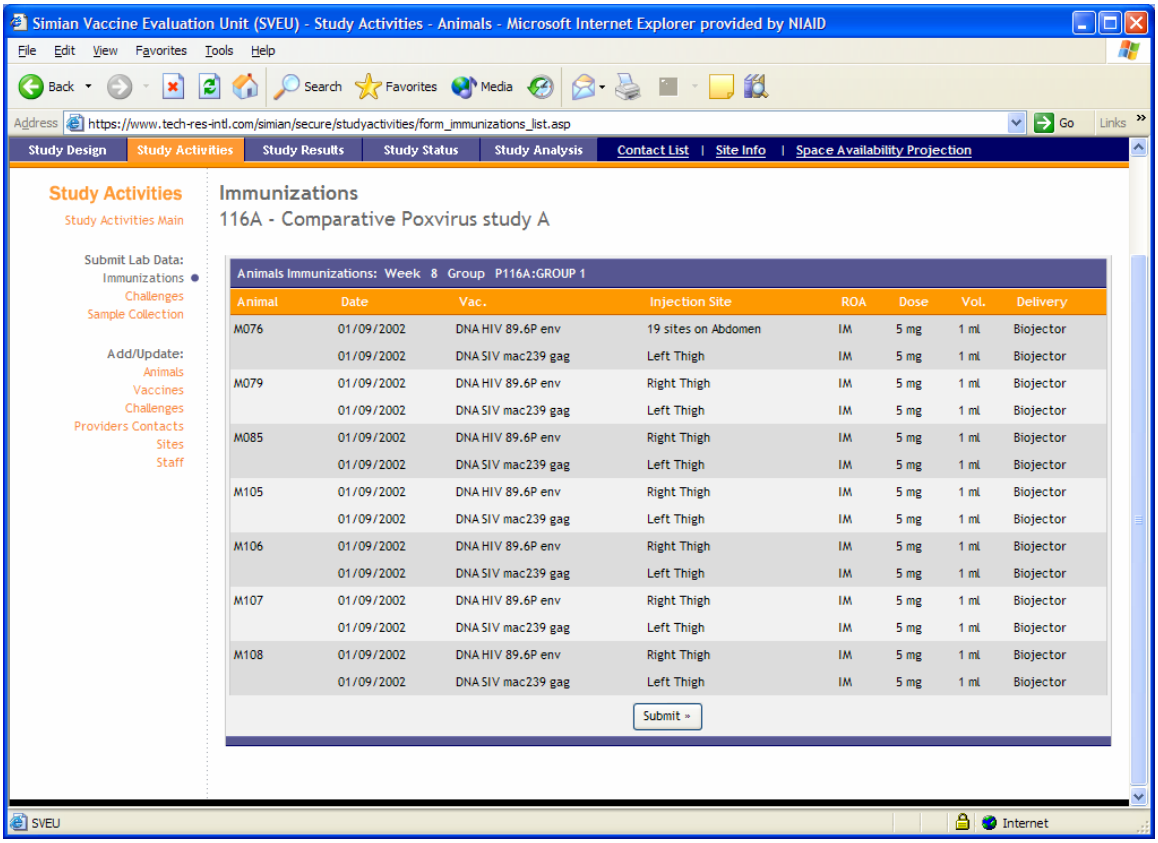
Add/Update:
Animals
Vaccines
Challenges
Providers Contacts
Sites
Staff
Immunizations
116A - Comparative Poxvirus study A
Animals Immunizations: Week 4 Group P116A:GROUP 2
Animal | Date | Vac. | Injection Site | ROA | Dose | Vol. | Delivery
M089 | 12/11/2001 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
12/11/2001 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
12/13/2001 | IL-2/Ig | L+R Quadriceps | IM | 5 mg | 1 ml | Biojector
M100 | 12/11/2001 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
12/11/2001 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
12/13/2001 | IL-2/Ig | L+R Quadriceps | IM | 5 mg | 1 ml | Biojector
M109 | 12/11/2001 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
12/11/2001 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
12/13/2001 | IL-2/Ig | L+R Quadriceps | IM | 5 mg | 1 ml | Biojector
M110 | 12/11/2001 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
12/11/2001 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
12/13/2001 | IL-2/Ig | L+R Quadriceps | IM | 5 mg | 1 ml | Biojector
M113 | 12/11/2001 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
12/11/2001 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
https://www.tech-res-intl.com/simian/secure/studyresults/default.asp
Internet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Immunizations
Challenges
Sample Collection
Add/Update:
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Vaccines
Challenges
Providers Contacts
Sites
Staff
Immunizations
116A - Comparative Poxvirus study A
Animals Immunizations: Week 8 Group P116A:GROUP 1
Animal Date Vac. Injection Site ROA Dose Vol. Delivery
M076 01/09/2002 DNA HIV 89.6P env 19 sites on Abdomen IM 5 mg 1 ml Biojector
01/09/2002 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
M079 01/09/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
01/09/2002 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
M085 01/09/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
01/09/2002 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
M105 01/09/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
01/09/2002 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
M106 01/09/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
01/09/2002 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
M107 01/09/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
01/09/2002 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
M108 01/09/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
01/09/2002 DNA SIV mac239 gag Left Thigh IM 5 mg 1 ml Biojector
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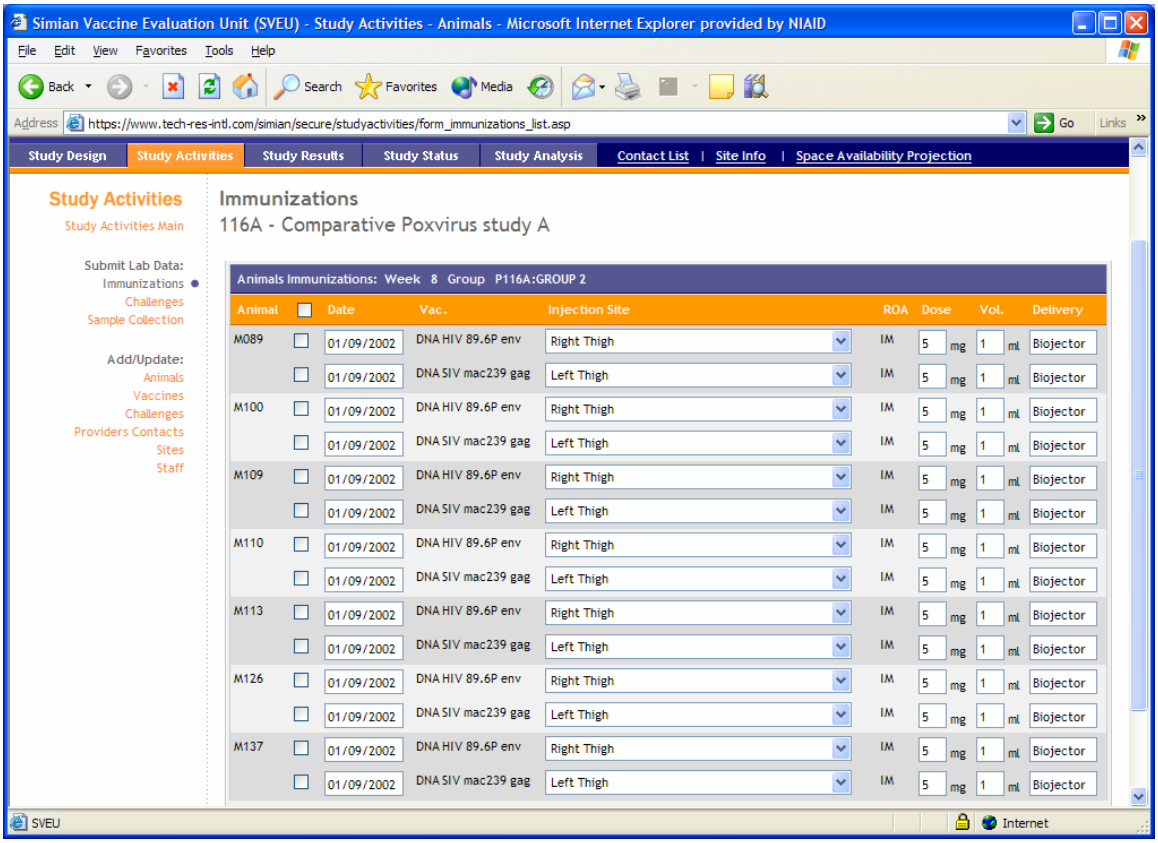
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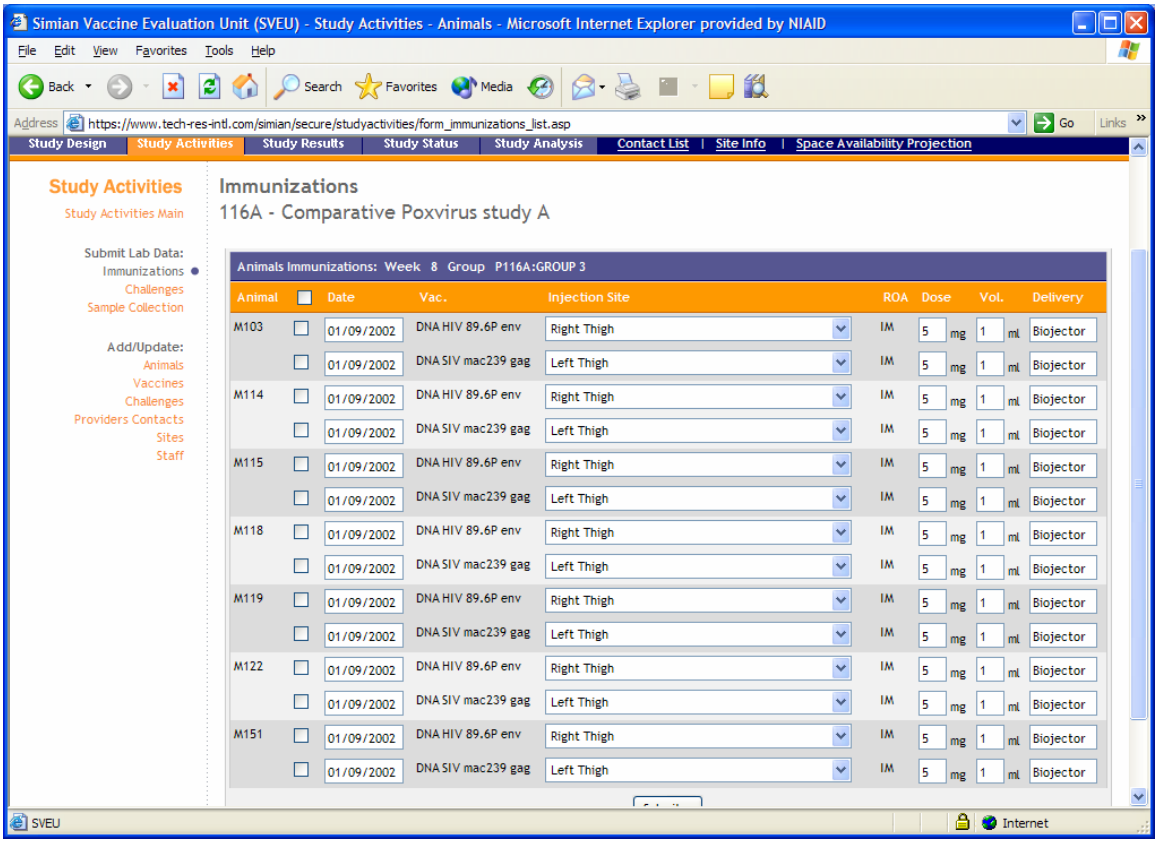
Vaccines
Challenges
Providers Contacts
Sites
Staff
Immunizations
116A - Comparative Poxvirus study A
Animals Immunizations: Week 8 Group P116A:GROUP 2
Animal | Date | Vac. | Injection Site | ROA | Dose | Vol. | Delivery
M089 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
M100 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
M109 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
M110 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
M113 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
M126 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
M137 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
SVEU
Internet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Immunizations
Challenges
Sample Collection
Add/Update:
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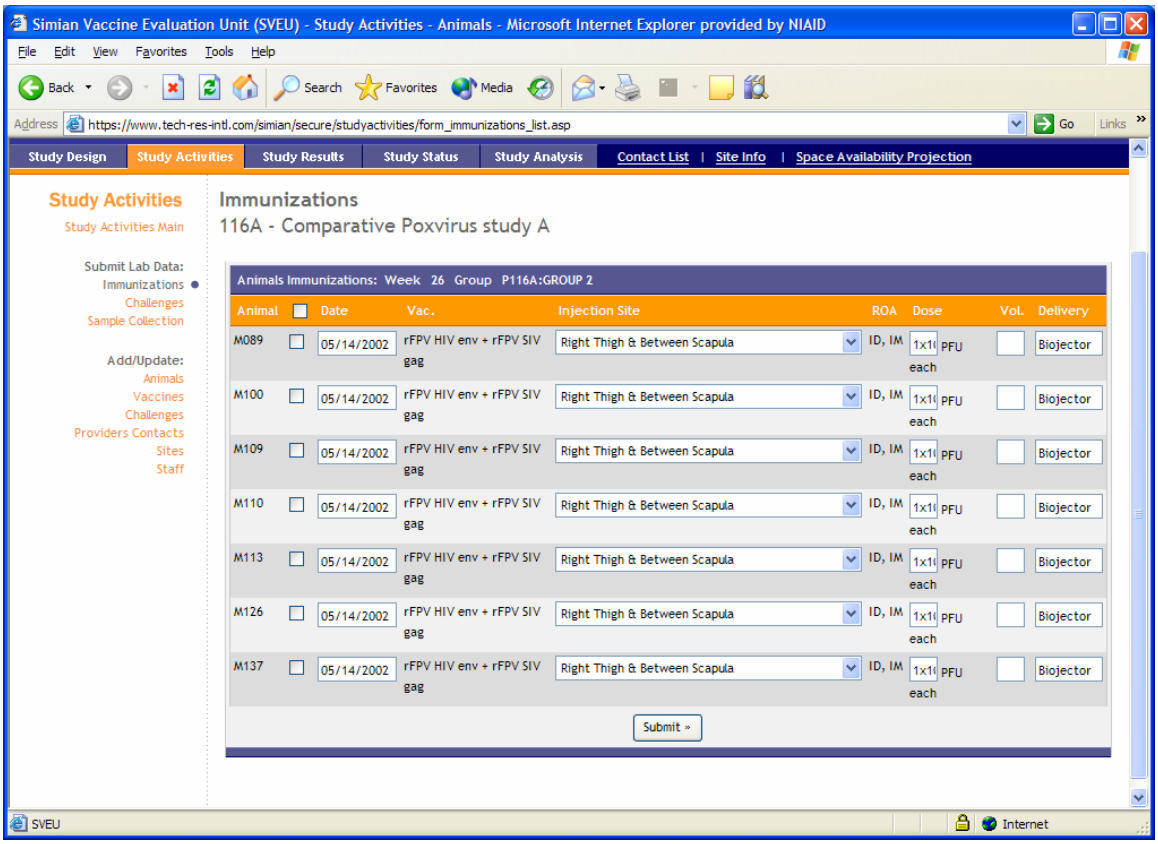
Vaccines
Challenges
Providers Contacts
Sites
Staff
Immunizations
116A - Comparative Poxvirus study A
Animals Immunizations: Week 8 Group P116A:GROUP 3
Animal | Date | Vac. | Injection Site | ROA | Dose | Vol. | Delivery
M103 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
M114 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
M115 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
M118 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
M119 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
M122 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
M151 | 01/09/2002 | DNA HIV 89.6P env | Right Thigh | IM | 5 mg | 1 ml | Biojector
01/09/2002 | DNA SIV mac239 gag | Left Thigh | IM | 5 mg | 1 ml | Biojector
SVEU
Internet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Immunizations
Challenges
Sample Collection
Add/Update:
Animals
Vaccines
Challenges
Providers Contacts
Sites
Staff
Immunizations
116A - Comparative Poxvirus study A
Animals Immunizations: Week 26 Group P116A:GROUP 2
Animal Date Vac. Injection Site ROA Dose Vol. Delivery
M089 05/14/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
M100 05/14/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
M109 05/14/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
M110 05/14/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
M113 05/14/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
M126 05/14/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
M137 05/14/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
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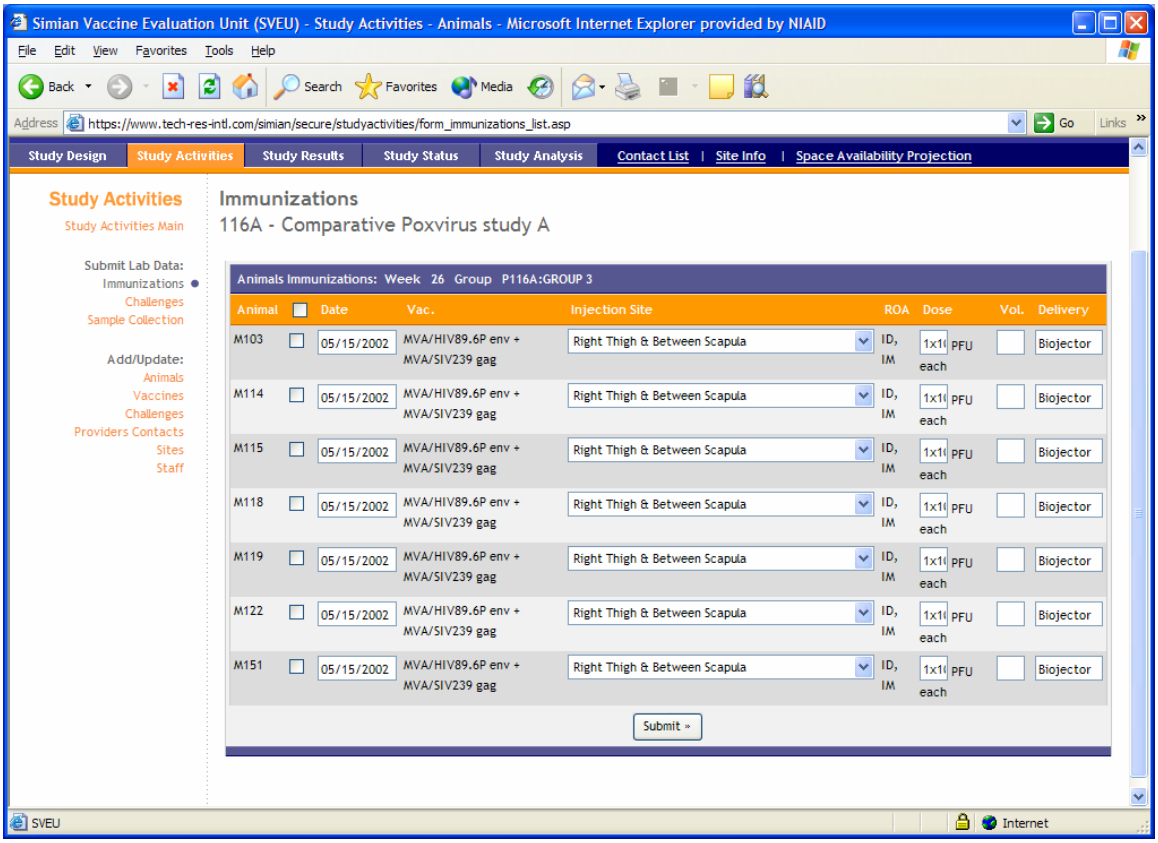
Internet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Study Activities
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Immunizations
Challenges
Sample Collection
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Animals
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Challenges
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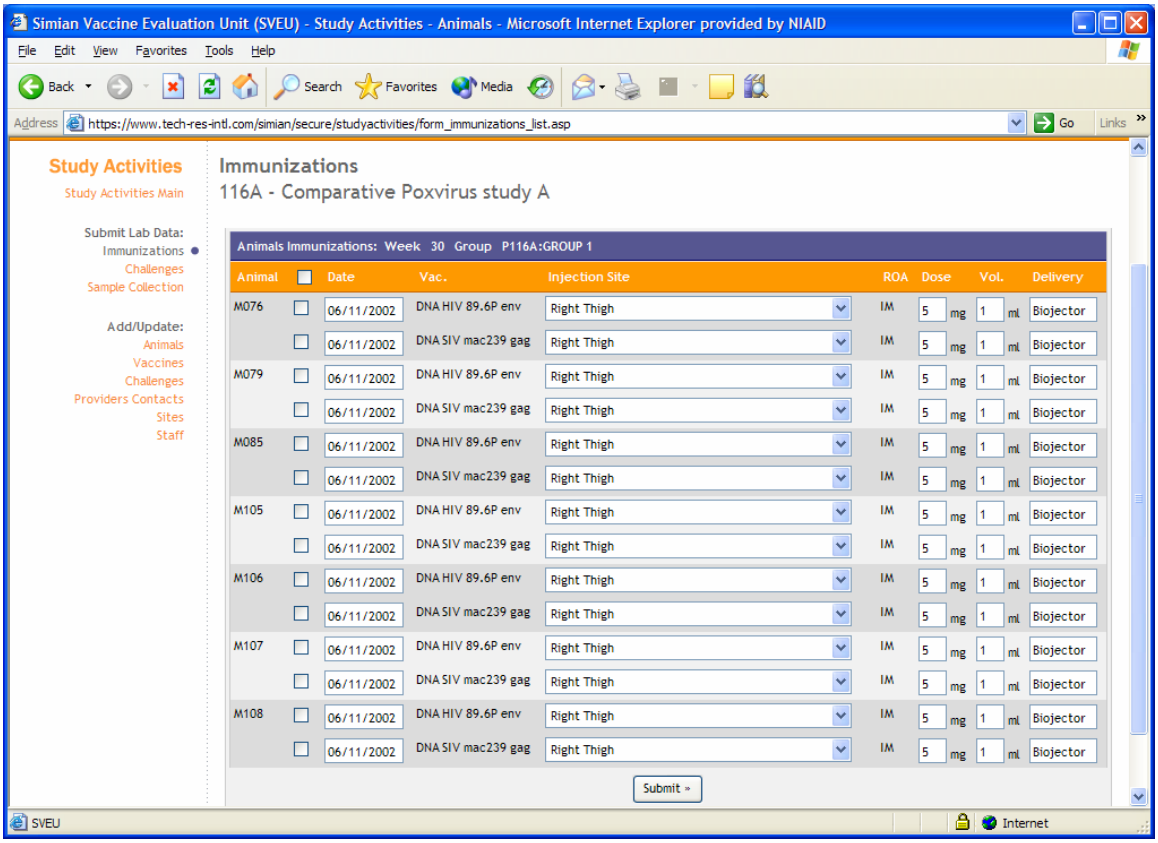
Immunizations
116A - Comparative Poxvirus study A
Animals Immunizations: Week 26 Group P116A:GROUP 3
Animal
Date
Vac.
Injection Site
ROA
Dose
Vol.
Delivery
M103 05/15/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
M114 05/15/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
M115 05/15/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
M118 05/15/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
M119 05/15/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
M122 05/15/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
M151 05/15/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each Biojector
Submit »
SVEU
Internet


Simian Vaccine Evaluation Unit (SVEU) - Study Activities - Animals - Microsoft Internet Explorer provided by NIAID
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Study Activities Main
Submit Lab Data:
Immunizations
Challenges
Sample Collection
Add/Update:
Animals
Vaccines
Challenges
Providers Contacts
Sites
Staff
Immunizations
116A - Comparative Poxvirus study A
Animals Immunizations: Week 30 Group P116A:GROUP 1
Animal Date Vac. Injection Site ROA Dose Vol. Delivery
M076 06/11/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
06/11/2002 DNA SIV mac239 gag Right Thigh IM 5 mg 1 ml Biojector
M079 06/11/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
06/11/2002 DNA SIV mac239 gag Right Thigh IM 5 mg 1 ml Biojector
M085 06/11/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
06/11/2002 DNA SIV mac239 gag Right Thigh IM 5 mg 1 ml Biojector
M105 06/11/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
06/11/2002 DNA SIV mac239 gag Right Thigh IM 5 mg 1 ml Biojector
M106 06/11/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
06/11/2002 DNA SIV mac239 gag Right Thigh IM 5 mg 1 ml Biojector
M107 06/11/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
06/11/2002 DNA SIV mac239 gag Right Thigh IM 5 mg 1 ml Biojector
M108 06/11/2002 DNA HIV 89.6P env Right Thigh IM 5 mg 1 ml Biojector
06/11/2002 DNA SIV mac239 gag Right Thigh IM 5 mg 1 ml Biojector
Submit »
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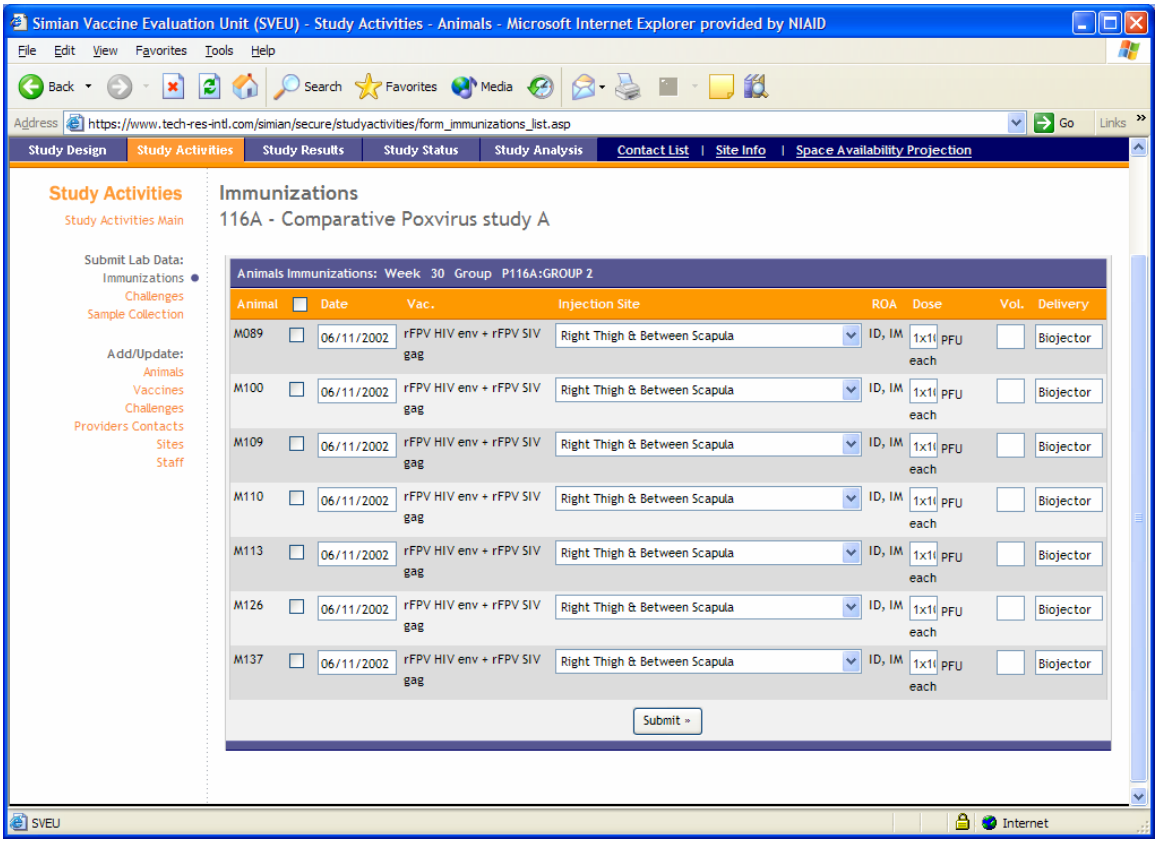
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Study Design Study Activities Study Results Study Status Study Analysis Contact List | Site Info | Space Availability Projection
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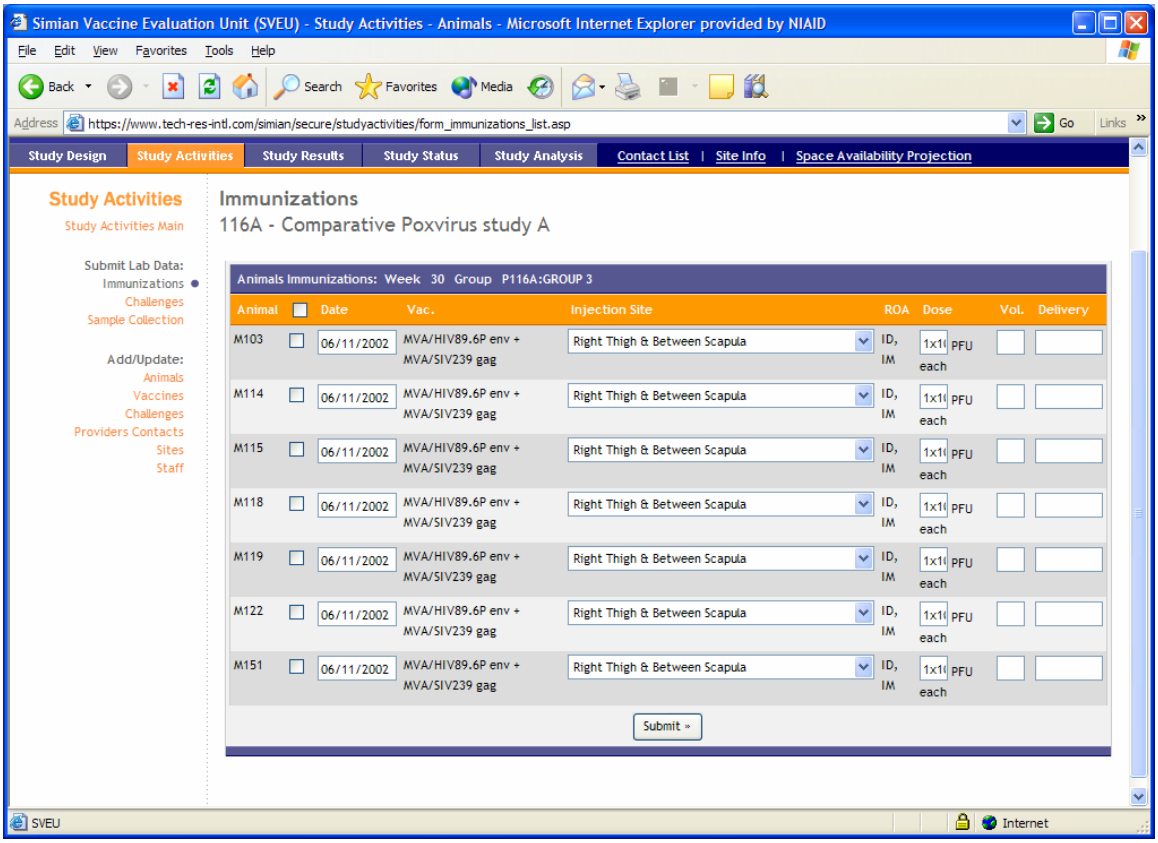
Study Activities Main
Submit Lab Data:
Immunizations
Challenges
Sample Collection
Add/Update:
Animals
Vaccines
Challenges
Providers Contacts
Sites
Staff
Immunizations
116A - Comparative Poxvirus study A
Animals Immunizations: Week 30 Group P116A:GROUP 2
Animal Date Vac. Injection Site ROA Dose Vol. Delivery
M089 06/11/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x10 PFU each Biojector
M100 06/11/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x10 PFU each Biojector
M109 06/11/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x10 PFU each Biojector
M110 06/11/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x10 PFU each Biojector
M113 06/11/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x10 PFU each Biojector
M126 06/11/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x10 PFU each Biojector
M137 06/11/2002 rFPV HIV env + rFPV SIV gag Right Thigh & Between Scapula ID, IM 1x10 PFU each Biojector
Submit »
SVEU
Internet


Simian Vaccine Evaluation Unit (SVEU) - Study Activities - Animals - Microsoft Internet Explorer provided by NIAID
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Study Activities Main
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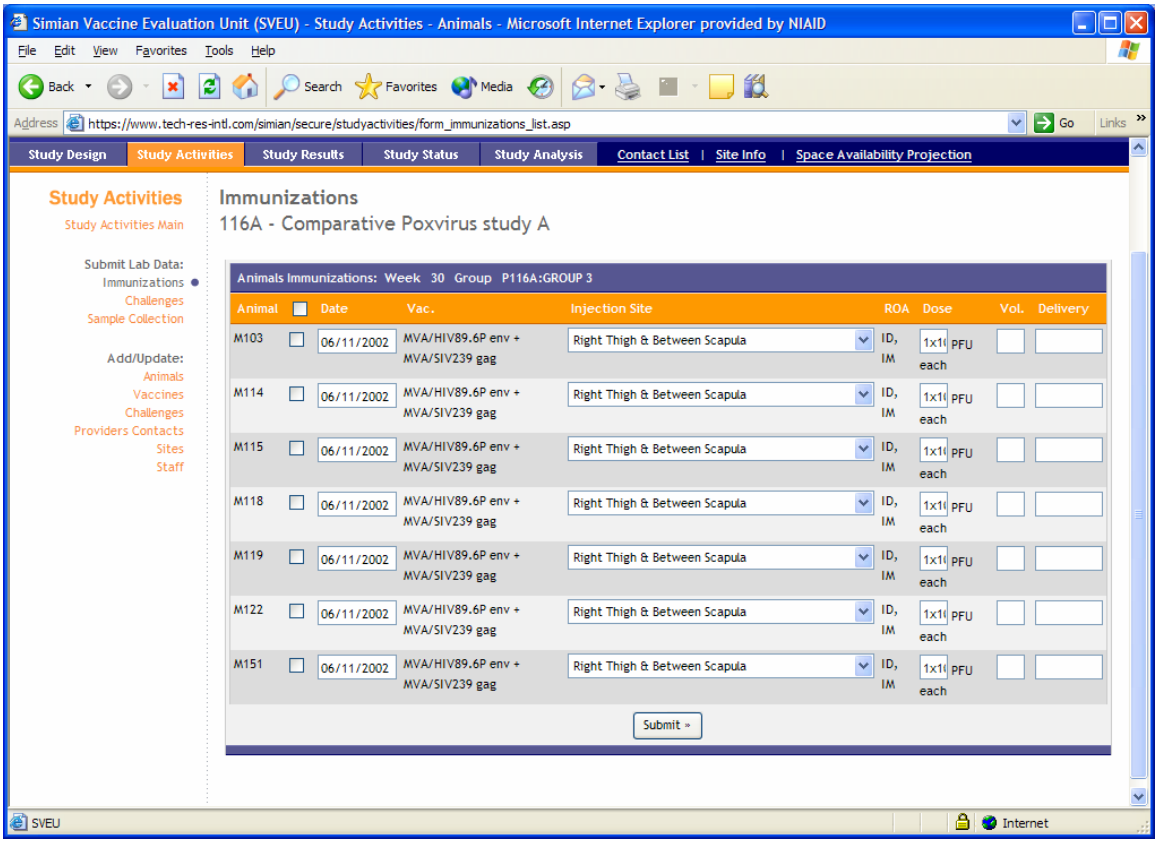
Immunizations
Challenges
Sample Collection
Add/Update:
Animals
Vaccines
Challenges
Providers Contacts
Sites
Staff
Immunizations
116A - Comparative Poxvirus study A
Animals Immunizations: Week 30 Group P116A:GROUP 3
Animal
Date
Vac.
Injection Site
ROA
Dose
Vol.
Delivery
M103 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1(PFU each
M114 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1(PFU each
M115 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1(PFU each
M118 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1(PFU each
M119 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1(PFU each
M122 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1(PFU each
M151 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1(PFU each
Submit »
SVEU
Internet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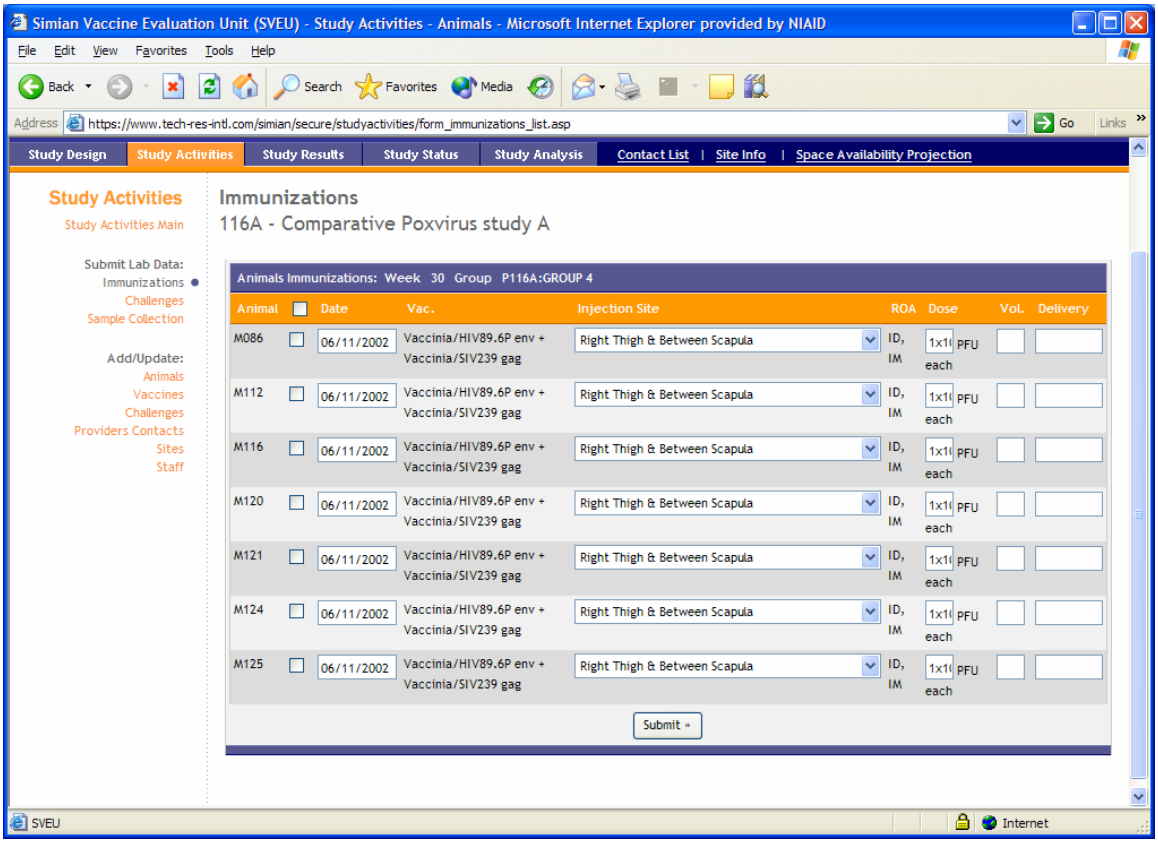
Contact List | Site Info | Space Availability Projection
Study Activities
Study Activities Main
Submit Lab Data:
Immunizations
Challenges
Sample Collection
Add/Update:
Animals
Vaccines
Challenges
Providers Contacts
Sites
Staff
Immunizations
116A - Comparative Poxvirus study A
Animals Immunizations: Week 30 Group P116A:GROUP 3
Animal
Date
Vac.
Injection Site
ROA
Dose
Vol.
Delivery
M103 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each
M114 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each
M115 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each
M118 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each
M119 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each
M122 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each
M151 06/11/2002 MVA/HIV89.6P env + MVA/SIV239 gag Right Thigh & Between Scapula ID, IM 1x1 PFU each
Submit »
SVEU
Internet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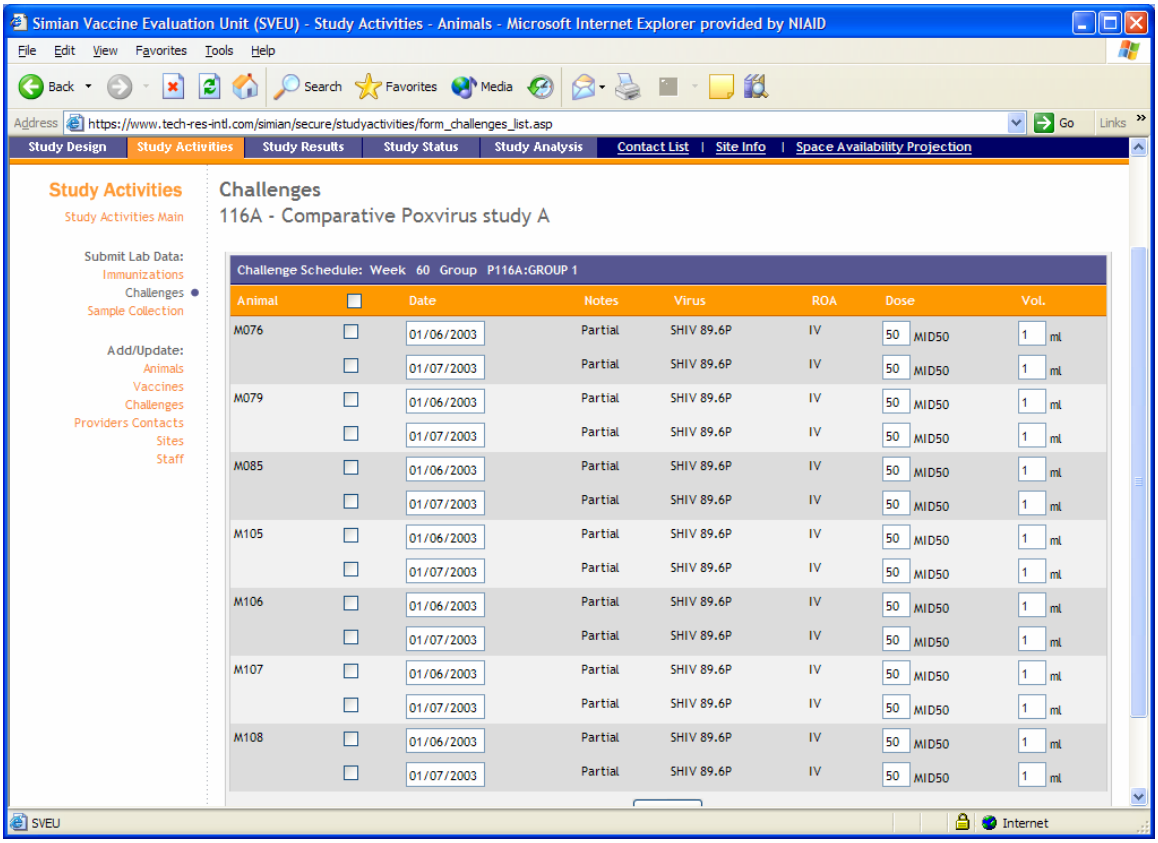
Study Activities
Study Activities Main
Submit Lab Data:
Immunizations
Challenges
Sample Collection
Add/Update:
Animals
Vaccines
Challenges
Providers Contacts
Sites
Staff
Immunizations
116A - Comparative Poxvirus study A
Animals Immunizations: Week 30 Group P116A:GROUP 4
Animal | Date | Vac. | Injection Site | ROA | Dose | Vol. | Delivery
M086 | 06/11/2002 | Vaccinia/HIV89.6P env + Vaccinia/SIV239 gag | Right Thigh & Between Scapula | ID, IM | 1x1(PFU each
M112 | 06/11/2002 | Vaccinia/HIV89.6P env + Vaccinia/SIV239 gag | Right Thigh & Between Scapula | ID, IM | 1x1(PFU each
M116 | 06/11/2002 | Vaccinia/HIV89.6P env + Vaccinia/SIV239 gag | Right Thigh & Between Scapula | ID, IM | 1x1(PFU each
M120 | 06/11/2002 | Vaccinia/HIV89.6P env + Vaccinia/SIV239 gag | Right Thigh & Between Scapula | ID, IM | 1x1(PFU each
M121 | 06/11/2002 | Vaccinia/HIV89.6P env + Vaccinia/SIV239 gag | Right Thigh & Between Scapula | ID, IM | 1x1(PFU each
M124 | 06/11/2002 | Vaccinia/HIV89.6P env + Vaccinia/SIV239 gag | Right Thigh & Between Scapula | ID, IM | 1x1(PFU each
M125 | 06/11/2002 | Vaccinia/HIV89.6P env + Vaccinia/SIV239 gag | Right Thigh & Between Scapula | ID, IM | 1x1(PFU each
Submit »
SVEU
Internet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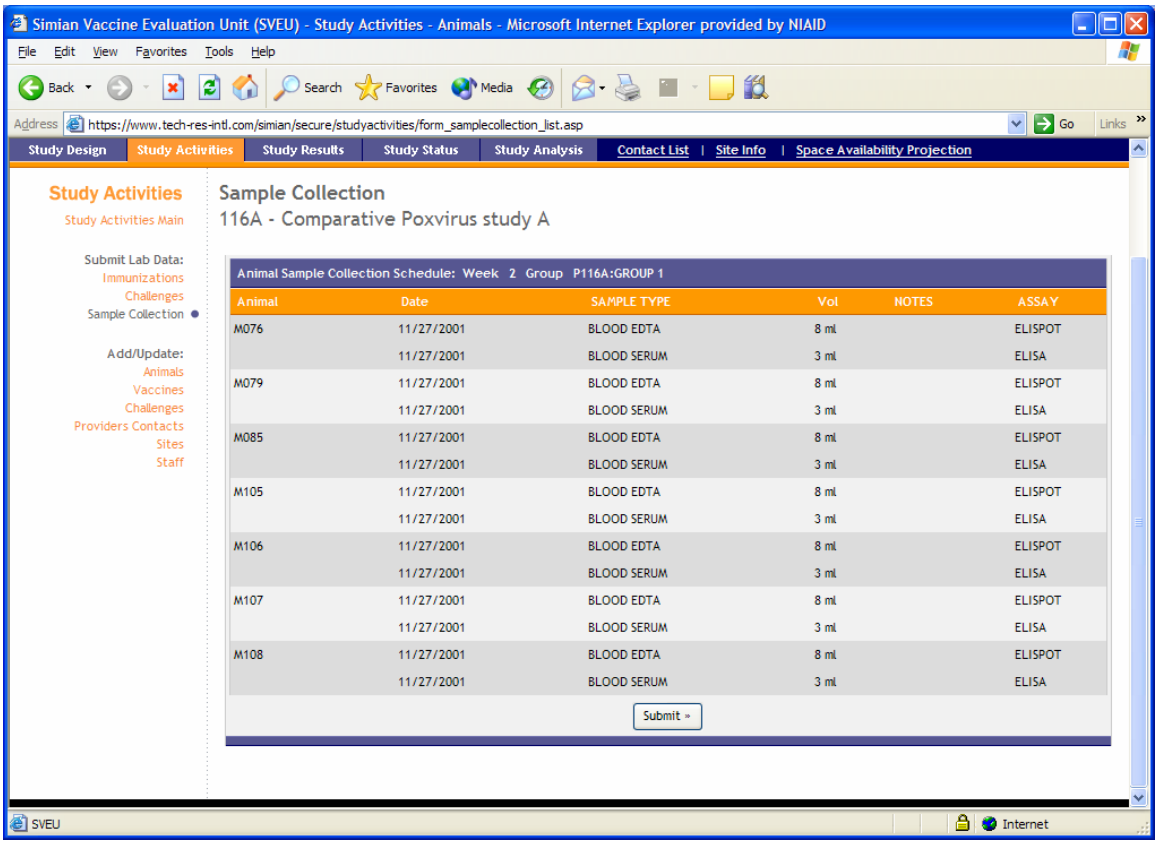
Study Design | Study Activities | Study Results | Study Status | Study Analysis | Contact List | Site Info | Space Availability Projection
Study Activities
Study Activities Main
Submit Lab Data:
Immunizations
Challenges
Sample Collection
Add/Update:
Animals
Vaccines
Challenges
Providers Contacts
Sites
Staff
Challenges
116A - Comparative Poxvirus study A
Challenge Schedule: Week 60 Group P116A:GROUP 1
Animal | Date | Notes | Virus | ROA | Dose | Vol.
M076 | 01/06/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
01/07/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
M079 | 01/06/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
01/07/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
M085 | 01/06/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
01/07/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
M105 | 01/06/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
01/07/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
M106 | 01/06/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
01/07/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
M107 | 01/06/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
01/07/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
M108 | 01/06/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
01/07/2003 | Partial | SHIV 89.6P | IV | 50 MID50 | 1 ml
SVEU
Internet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Study Results
Study Status
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Contact List | Site Info | Space Availability Projection
Study Activities
Study Activities Main
Submit Lab Data:
Immunizations
Challenges
Sample Collection
Add/Update:
Animals
Vaccines
Challenges
Providers Contacts
Sites
Staff
Sample Collection
116A - Comparative Poxvirus study A
Animal Sample Collection Schedule: Week 2 Group P116A:GROUP 1
Animal Date SAMPLE TYPE Vol NOTES ASSAY
M076 11/27/2001 BLOOD EDTA 8 ml ELISPOT
11/27/2001 BLOOD SERUM 3 ml ELISA
M079 11/27/2001 BLOOD EDTA 8 ml ELISPOT
11/27/2001 BLOOD SERUM 3 ml ELISA
M085 11/27/2001 BLOOD EDTA 8 ml ELISPOT
11/27/2001 BLOOD SERUM 3 ml ELISA
M105 11/27/2001 BLOOD EDTA 8 ml ELISPOT
11/27/2001 BLOOD SERUM 3 ml ELISA
M106 11/27/2001 BLOOD EDTA 8 ml ELISPOT
11/27/2001 BLOOD SERUM 3 ml ELISA
M107 11/27/2001 BLOOD EDTA 8 ml ELISPOT
11/27/2001 BLOOD SERUM 3 ml ELISA
M108 11/27/2001 BLOOD EDTA 8 ml ELISPOT
11/27/2001 BLOOD SERUM 3 ml ELISA
Submit »
SVEU
Internet

ABSTRACT OF THE PUBLISHED STUDY:

Recombinant poxvirus boosting of DNA-primed rhesus monkeys augments peak but not memory T lymphocyte responses.

Santra S, Barouch DH, Korioth-Schmitz B, Lord CI, Krivulka GR, Yu F, Beddall MH, Gorgone DA, Lifton MA, Miura A, Philippon V, Manson K, Markham PD, Parrish J, Kuroda MJ, Schmitz JE, Gelman RS, Shiver JW, Montefiori DC, Panicali D, Letvin NL.

Division of Viral Pathogenesis, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02115, USA.

Although a consensus has emerged that an HIV vaccine should elicit a cytotoxic T lymphocyte (CTL) response, the characteristics of an effective vaccine-induced T lymphocyte response remain unclear. We explored this issue in the simian human immunodeficiency virus/rhesus monkey model in the course of assessing the relative immunogenicity of vaccine regimens that included a cytokine-augmented plasmid DNA prime and a boost with DNA or recombinant pox vectors. Recombinant vaccinia virus, recombinant modified vaccinia Ankara (MVA), and recombinant fowlpox were comparable in their immunogenicity. Moreover, whereas the magnitude of the peak vaccine-elicited T lymphocyte responses in the recombinant pox virus-boosted monkeys was substantially greater than that seen in the monkeys immunized with plasmid DNA alone, the magnitudes of recombinant pox boosted CTL responses decayed rapidly and were comparable to those of the DNA-alone-vaccinated monkeys by the time of viral challenge. Consistent with these comparable memory T cell responses, the clinical protection seen in all groups of experimentally vaccinated monkeys was similar. This study, therefore, indicates that the steady-state memory, rather than the peak effector vaccine-elicited T lymphocyte responses, may be the critical immune correlate of protection for a CTL-based HIV vaccine.

Reference: Proc. Natl. Acad. Sci. (2004) **101**, 11088-11093

LINK TO FULL TEXT OF THE PUBLISHED STUDY:

http--www.pubmedcentral.nih.gov-picrender.fcgiartid=503745&action=stream&blobtype=pdf.url

APPENDIX C

EXAMPLES OF PUBLICATIONS RESULTING FROM AIDS VACCINE STUDIES CONDUCTED BY THE SVEUS

1) Proc Natl Acad Sci U S A. 2004 Jul 27;101(30):11088-93. Epub 2004 Jul 16.

Recombinant poxvirus boosting of DNA-primed rhesus monkeys augments peak but not memory T lymphocyte responses.

Santra S, Barouch DH, Korioth-Schmitz B, Lord CI, Krivulka GR, Yu F, Beddall MH, Gorgone DA, Lifton MA, Miura A, Philippon V, Manson K, Markham PD, Parrish J, Kuroda MJ, Schmitz JE, Gelman RS, Shiver JW, Montefiori DC, Panicali D, Letvin NL.

Division of Viral Pathogenesis, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02115, USA.

Although a consensus has emerged that an HIV vaccine should elicit a cytotoxic T lymphocyte (CTL) response, the characteristics of an effective vaccine-induced T lymphocyte response remain unclear. We explored this issue in the simian human immunodeficiency virus/rhesus monkey model in the course of assessing the relative immunogenicity of vaccine regimens that included a cytokine-augmented plasmid DNA prime and a boost with DNA or recombinant pox vectors. Recombinant vaccinia virus, recombinant modified vaccinia Ankara (MVA), and recombinant fowlpox were comparable in their immunogenicity. Moreover, whereas the magnitude of the peak vaccine-elicited T lymphocyte responses in the recombinant pox virus-boosted monkeys was substantially greater than that seen in the monkeys immunized with plasmid DNA alone, the magnitudes of recombinant pox boosted CTL responses decayed rapidly and were comparable to those of the DNA-alone-vaccinated monkeys by the time of viral challenge. Consistent with these comparable memory T cell responses, the clinical protection seen in all groups of experimentally vaccinated monkeys was similar. This study, therefore, indicates that the steady-state memory, rather than the peak effector vaccine-elicited T lymphocyte responses, may be the critical immune correlate of protection for a CTL-based HIV vaccine.

2) Immunol Lett. 2001 Nov 1;79(1-2):57-61.

Vaccine-elicited immune responses prevent clinical AIDS in SHIV(89.6P)-infected rhesus monkeys.

Barouch DH, Fu TM, Montefiori DC, Lewis MG, Shiver JW, Letvin NL.

Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, 330 Brookline Avenue, Boston, MA 02215, USA. dan_barouch@hotmail.com

Accumulating evidence has demonstrated the importance of cytotoxic T lymphocytes (CTLs) and helper T lymphocytes in controlling HIV-1 replication. We have elicited immune responses in rhesus monkeys utilizing DNA vaccines augmented by the administration of IL-2/Ig, a fusion protein consisting of interleukin-2 and the Fc portion of IgG2. These vaccine-elicited immune responses did not prevent infection following a high-dose intravenous challenge with SHIV(89.6P) but did control viremia to nearly undetectable levels and prevented immunodeficiency and clinical disease. In contrast, control monkeys developed high levels of viremia and exhibited a rapid loss of CD4(+) T cells, significant clinical disease progression, and death in half of the animals by day 140 following challenge. Vaccine approaches that elicit immune responses capable of reducing plasma viral loads, but not capable of inducing sterilizing immunity, may still provide substantial clinical benefits.

3) J Virol. 2003 Jul;77(13):7367-75.

Viral escape from dominant simian immunodeficiency virus epitope-specific cytotoxic T lymphocytes in DNA-vaccinated rhesus monkeys.

Barouch DH, Kunstman J, Glowczwskie J, Kunstman KJ, Egan MA, Peyerl FW, Santra S, Kuroda MJ, Schmitz JE, Beaudry K, Krivulka GR, Lifton MA, Gorgone DA, Wolinsky SM, Letvin NL.

Division of Viral Pathogenesis, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts 02215, USA. dbarouch@bidmc.harvard.edu

Virus-specific cytotoxic T lymphocytes (CTL) are critical for control of human immunodeficiency virus type 1 replication. However, viral escape from CTL recognition can undermine this immune control. Here we demonstrate the high frequency and pattern of viral escape from dominant epitope-specific CTL in SIV gag DNA-vaccinated rhesus monkeys following a heterologous simian immunodeficiency virus (SIV) challenge. DNA-vaccinated monkeys exhibited initial effective control of the SIV challenge, but this early control was lost by serial breakthroughs of viral replication over a 3-year follow-up period. Increases in plasma viral RNA correlated temporally with declines of dominant SIV epitope-specific CD8(+) T-lymphocyte responses and the emergence of viral mutations that escaped recognition by dominant epitope-specific CTL. Viral escape from CTL occurred in a total of seven of nine vaccinated and control monkeys, including three animals that initially controlled viral replication to undetectable levels of plasma viral RNA. These data suggest that CTL exert selective pressure on viral replication and that viral escape from CTL may be a limitation of CTL-based AIDS vaccine strategies.

4) J Virol. 2001 Jan;75(2):645-53.

Immunogenicity and protective efficacy of oligomeric human immunodeficiency virus type 1 gp140.

Earl PL, Sugiura W, Montefiori DC, Broder CC, Lee SA, Wild C, Lifson J, Moss B.

Laboratory of Viral Diseases, NIAID, National Institutes of Health, Bethesda, Maryland 20892-0455, USA. pearl@nih.gov

The biologically active form of the human immunodeficiency virus type 1 (HIV-1) envelope (Env) glycoprotein is oligomeric. We previously described a soluble HIV-1 IIIB Env protein, gp140, with a stable oligomeric structure composed of uncleaved gp120 linked to the ectodomain of gp41 (P. L. Earl, C. C. Broder, D. Long, S. A. Lee, J. Peterson, S. Chakrabarti, R. W. Doms, and B. Moss, J. Virol. 68:3015-3026, 1994). Here we compared the antibody responses of rabbits to gp120 and gp140 that had been produced and purified in an identical manner. The gp140 antisera exhibited enhanced cross-reactivity with heterologous Env proteins as well as greater neutralization of HIV-1 compared to the gp120 antisera. To examine both immunogenicity and protective efficacy, we immunized rhesus macaques with oligomeric gp140. Strong neutralizing antibodies against a homologous virus and modest neutralization of heterologous laboratory-adapted isolates were elicited. No neutralization of primary isolates was observed. However, a substantial fraction of the neutralizing activity could not be blocked by a V3 loop peptide. After intravenous challenge with simian-HIV virus SHIV-HXB2, three of the four vaccinated macaques exhibited no evidence of virus replication.

5) Virology. 2002 Mar 15;294(2):270-81.

Comparison of vaccine strategies using recombinant env-gag-pol MVA with or without an oligomeric Env protein boost in the SHIV rhesus macaque model.

Earl PL, Wyatt LS, Montefiori DC, Bilska M, Woodward R, Markham PD, Malley JD, Vogel TU, Allen TM, Watkins DI, Miller N, Moss B.

Laboratory of Viral Diseases, National Institutes of Allergy and Infectious Diseases, Bethesda, Maryland 20892,

USA. pearl@atlas.niaid.nih.gov

Rhesus macaques were immunized with a replication-deficient vaccinia virus (MVA) expressing human immunodeficiency virus type 1 89.6 envelope (env) and SIV gagpol (MVA/SHIV89.6) with or without a protein boost consisting of soluble 89.6 env (gp140). Immunization with MVA/SHIV89.6 alone elicited binding antibodies in all animals and neutralizing antibodies in 5 of 15 animals. Both types of antibodies were enhanced by protein boosting. In addition, CD8 cells exhibiting CM9 tetramer binding were detected in the subset of animals that were Mamu-A*01 positive. Animals were challenged intravenously with either SHIV-89.6 (Study 1) or the more pathogenic derivative SHIV-89.6P (Study 2). In Study 1, all control and vaccinated animals except one became infected. However, the levels of viremia were as follows: controls > rMVA alone > rMVA + protein. The differences were statistically significant between immunized and control groups but not between the two immunized groups. In Study 2, all animals became infected; however, the vaccinated group exhibited a 5-fold reduction in peak viremia and a 10-fold reduction in the postacute phase viremia in comparison to the controls. All of the controls required euthanasia by 10 months after challenge. A relationship between vaccine-induced antibody titers and reduction in virus burden was observed in both studies. Thus, immunization with MVA/SHIV89.6 alone or with a protein boost stimulated both arms of the immune system and resulted in significant control of viremia and delayed progression to disease after challenge with SHIV-89.6P.

6) J Invest Dermatol. 2005 Jan;124(1):160-9.

DermaVir: a novel topical vaccine for HIV/AIDS.

Lisziewicz J, Trocio J, Whitman L, Varga G, Xu J, Bakare N, Erbacher P, Fox C, Woodward R, Markham P, Arya S, Behr JP, Lori F.

Research Institute for Genetic and Human Therapy (RIGHT), Washington, DC 20007, USA. lisziewj@geneticimmunity.com

Human immunodeficiency virus (HIV) vaccines have the potential to improve antiretroviral drug treatment by inducing cytotoxic killing of HIV-infected cells. Prophylactic vaccines utilize new antigens to initiate immunity; however, in HIV-infected individuals the load of viral antigen is not the limiting factor for the restoration of immune responses. Here we describe a novel immunization strategy with DermaVir that improves viral antigen presentation using dendritic cells (DC). DermaVir contains a distinctive plasmid DNA expressing all HIV proteins except integrase to induce immune responses with broad specificity. The DNA is formulated to a mannosilated particle to target antigen-presenting cells and to protect the DNA from intracellular degradation. After topical application, DermaVir-transduced cells migrate from the skin to the draining lymph node and interdigitate as DermaVir-expressing, antigen-presenting DC. We compared the immunogenicity of topical and ex vivo DC-based DermaVir vaccinations in naive rhesus macaques. Both vaccinations induced simian immunodeficiency virus-specific CD4 helper and CD8 memory T cells detected by an in vivo skin test and an in vitro intracellular cytokine-based assay. Topical DermaVir vaccination represents an improvement upon existing ex vivo DC-based immunization technologies and may provide a new therapeutic option for HIV-infected patients.

7) Proc Natl Acad Sci U S A. 2002 Sep 3;99(18):11842-7. Epub 2002 Aug 21.

Crosslinked HIV-1 envelope-CD4 receptor complexes elicit broadly cross-reactive neutralizing antibodies in rhesus macaques.

Fouts T, Godfrey K, Bobb K, Montefiori D, Hanson CV, Kalyanaraman VS, DeVico A, Pal R.

Institute of Human Virology, University of Maryland Biotechnology Institute, 725 West Lombard Street, Baltimore, MD 21201, USA.

The identification of HIV envelope structures that generate broadly cross-reactive neutralizing antibodies is a major goal for HIV-vaccine development. In this study, we evaluated one such structure, expressed as either a gp120-CD4 or a gp140-CD4 complex, for its ability to elicit a neutralizing antibody response. In rhesus macaques, covalently crosslinked complexes of soluble human CD4 (shCD4) and HIV-1(IIIB) envelope glycoproteins (gp120 or gp140) generated antibodies that neutralized a wide range of primary HIV-1 isolates regardless of the coreceptor usage or

genetic subtype. Ig with cross-reactive neutralizing activity was recovered by affinity chromatography with a chimeric single-chain polypeptide containing sequences for HIV(BaL) gp120 and a mimetic peptide that induces a CD4-triggered envelope structure. These results suggest that covalently crosslinked complexes of the HIV-1 surface envelope glycoprotein and CD4 elicit broadly neutralizing humoral responses that, in part, may be directed against a novel epitope(s) found on the HIV-1 envelope.

8) J Virol. 1996 Jun;70(6):3724-33.

Vaccine protection by a triple deletion mutant of simian immunodeficiency virus.

Wyand MS, Manson KH, Garcia-Moll M, Montefiori D, Desrosiers RC.

TSI Mason Laboratory, Worcester, Massachusetts, USA.

Twelve rhesus monkeys were vaccinated with SIVmac316 delta nef (lacking nef sequences), and 12 were vaccinated with SIVmac239 delta3 (lacking nef, vpr, and upstream sequences in U3). SIVmac316 and SIVmac239 differ by only eight amino acids in the envelope; these changes render SIVmac316 highly competent for replication in macrophages. Seventeen of the animals developed persistent infections with the vaccine viruses. Seven of the 24 vaccinated animals, however, developed infections that were apparently transient in nature. Six of these seven yielded virus from peripheral blood when tested at weeks 2 and/or 3, three of the seven had transient antibody responses, but none of the seven had persisting antibody responses. The 24 monkeys were challenged in groups of four with 10 rhesus monkey infectious doses of wild-type, pathogenic SIVmac251 at weeks 8, 20, and 79 following receipt of vaccine. None of the seven with apparently transient infections with vaccine virus were protected upon subsequent challenge. Analysis of cell-associated viral loads, CD4+ cell counts, and viral gene sequences present in peripheral blood in the remainder of the monkeys following challenge allowed a number of conclusions. (i) There was a trend toward increased protection with length of time of vaccination. (ii) Solid vaccine protection was achieved by 79 weeks with the highly attenuated SIV239 delta3. (iii) Solid long-term protection was achieved in at least two animals in the absence of complete sterilizing immunity. (iv) Genetic backbone appeared to influence protective capacity; animals vaccinated with SIV239 delta3 were better protected than animals receiving SIV316 delta nef. This better protection correlated with increased levels of the replicating vaccine strain. (v) The titer of virus-neutralizing activity in serum on the day of challenge correlated with protection when measured against a primary stock of SIVmac251 but not when measured against a laboratory-passaged stock. The level of binding antibodies to whole virus by enzyme-linked immunosorbent assay also correlated with protection.

9) J Virol. 1999 Oct;73(10):8356-63.

Protection by live, attenuated simian immunodeficiency virus against heterologous challenge.

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We examined the ability of a live, attenuated deletion mutant of simian immunodeficiency virus (SIV), SIVmac239Delta3, which is missing nef and vpr genes, to protect against challenge by heterologous strains SHIV89.6p and SIVsmE660. SHIV89.6p is a pathogenic, recombinant SIV in which the envelope gene has been replaced by a human immunodeficiency virus type 1 envelope gene; other structural genes of SHIV89.6p are derived from SIVmac239. SIVsmE660 is an uncloned, pathogenic, independent isolate from the same primate lentivirus subgrouping as SIVmac but with natural sequence variation in all structural genes. The challenge with SHIV89.6p was performed by the intravenous route 37 months after the time of vaccination. By the criteria of CD4(+) cell counts and disease, strong protection against the SHIV89.6p challenge was observed in four of four vaccinated monkeys despite the complete mismatch of env sequences. However, SHIV89.6p infection was established in all four previously vaccinated monkeys and three of the four developed fluctuating viral loads between 300 and 10,000 RNA copy equivalents per ml of plasma 30 to 72 weeks postchallenge. When other vaccinated monkeys were challenged with SIVsmE660 at 28 months after the time of vaccination, SIV loads were lower than those observed in unvaccinated controls but the level of protection was less than what was observed against SHIV89.6p in these experiments and considerably less than the level of protection against SIVmac251 observed in previous experiments.

These results demonstrate a variable level of vaccine protection by live, attenuated SIVmac239Delta3 against heterologous virus challenge and suggest that even live, attenuated vaccine approaches for AIDS will face significant hurdles in providing protection against the natural variation present in field strains of virus. The results further suggest that factors other than anti-Env immune responses can be principally responsible for the vaccine protection by live, attenuated SIV.

10) J Virol. 1999 Jun;73(6):4952-61.

Highly attenuated vaccine strains of simian immunodeficiency virus protect against vaginal challenge: inverse relationship of degree of protection with level of attenuation.

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Three different deletion mutants of simian immunodeficiency virus (SIV) that vary in their levels of attenuation were tested for the ability to protect against mucosal challenge with pathogenic SIV. Four female rhesus monkeys were vaccinated by intravenous inoculation with SIVmac239Delta3, four with SIVmac239Delta3X, and four with SIVmac239Delta4. These three vaccine strains exhibit increasing levels of attenuation: Delta3 < Delta3X <Delta4. The vaccinated monkeys were challenged by vaginal exposure to uncloned, pathogenic SIVmac251 at 61 weeks after the time of vaccination. On the basis of viral RNA loads in plasma, cell-associated virus loads in peripheral blood, and CD4 cell counts, strong protective effects were observed in all three groups of vaccinated monkeys. However, the degree of protection correlated inversely with the level of attenuation; the least-attenuated strain, SIVmac239Delta3, gave the greatest protection. One monkey in the Delta3X group and two in the Delta4 group clearly became superinfected by the challenge virus, but these animals had levels of SIV RNA in plasma that were considerably lower than those of naive animals that were challenged in parallel. Protection against vaginal challenge appears easier to achieve than protection against intravenous challenge, since four other SIVmac239Delta4-vaccinated monkeys showed no protection when challenged intravenously with a much lower inoculum of the same challenge virus stock. Protection against vaginal challenge in the Delta4-vaccinated group occurred in the absence of detectable serum neutralizing activities and appeared to be associated with the development of an early SIV-specific cytotoxic-T-lymphocyte response. Our results demonstrate that mucosal protection can be achieved by systemic immunization with the highly attenuated SIVmac239Delta4 more than 1 year prior to the time of challenge.

11) J Virol. 1996 Jun;70(6):3978-91.

Simian immunodeficiency virus DNA vaccine trial in macaques.

Lu S, Arthos J, Montefiori DC, Yasutomi Y, Manson K, Mustafa F, Johnson E, Santoro JC, Wissink J, Mullins JI, Haynes JR, Letvin NL, Wyand M, Robinson HL.

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An experimental vaccine consisting of five DNA plasmids expressing different combinations and forms of simian immunodeficiency virus-macaque (SIVmac) proteins has been evaluated for the ability to protect against a highly pathogenic uncloned SIVmac251 challenge. One vaccine plasmid encoded nonreplicating SIVmac239 virus particles. The other four plasmids encoded secreted forms of the envelope glycoproteins of two T-cell-tropic relatives (SIVmac239 and SIVmac251) and one monocyte/macrophage-tropic relative (SIVmac316) of the uncloned challenge virus. Rhesus macaques were inoculated with DNA at 1 and 3, 11 and 13, and 21 and 23 weeks. Four macaques were inoculated intravenously, intramuscularly, and by gene gun inoculations. Three received only gene gun inoculations. Two control monkeys were inoculated with control plasmids by all three routes of inoculation. Neutralizing antibody titers of 1:216 to 1:768 were present in all of the vaccinated monkeys after the second cluster

of inoculations. These titers were transient, were not boosted by the third cluster of inoculations, and had fallen to 1:24 to 1:72 by the time of challenge. Cytotoxic T-cell activity for Env was also raised in all of the vaccinated animals. The temporal appearance of cytotoxic T cells was similar to that of antibody. However, while antibody responses fell with time, cytotoxic T-cell responses persisted. The SIVmac251 challenge was administered intravenously at 2 weeks following the last immunization. The DNA immunizations did not prevent infection or protect against CD4+ cell loss. Long-term chronic levels of infection were similar in the vaccinated and control animals, with 1 in 10,000 to 1 in 100,000 peripheral blood cells carrying infectious virus. However, viral loads were reduced to the chronic level over a shorter period of time in the vaccinated groups (6 weeks) than in the control group (12 weeks). Thus, the DNA vaccine raised both neutralizing antibody and cytotoxic T-lymphocyte responses and provided some attenuation of the acute phase of infection, but it did not prevent the loss of CD4+ cells.

12) J Virol. 1996 Jan;70(1):678-81.

Simian immunodeficiency virus-specific cytotoxic T-lymphocyte induction through DNA vaccination of rhesus monkeys.

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In view of the growing evidence that virus-specific cytotoxic T lymphocytes (CTL) play an important role in containing the early spread of human immunodeficiency virus type 1 (HIV-1) in infected individuals, novel vaccine strategies capable of eliciting HIV-1-specific CTL are being pursued in attempts to create an effective AIDS vaccine. We have used the simian immunodeficiency virus of macaques (SIVmac)/rhesus monkey model to explore the induction of AIDS virus-specific CTL responses by DNA vaccination. We found that the inoculation of rhesus monkeys with plasmid DNA encoding SIVmac Env and Gag elicited a persisting SIVmac-specific memory CTL response. These CTL were CD8+ and major histocompatibility complex class I restricted. These studies provide evidence for the potential utility of DNA inoculation as an approach to an HIV-1 vaccine.

13) Nat Med. 1999 May;5(5):526-34.

Neutralizing antibody-independent containment of immunodeficiency virus challenges by DNA priming and recombinant pox virus booster immunizations.

Robinson HL, Montefiori DC, Johnson RP, Manson KH, Kalish ML, Lifson JD, Rizvi TA, Lu S, Hu SL, Mazzara GP, Panicali DL, Herndon JG, Glickman R, Candido MA, Lydy SL, Wyand MS, McClure HM.

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Eight different protocols were compared for their ability to raise protection against immunodeficiency virus challenges in rhesus macaques. The most promising containment of challenge infections was achieved by intradermal DNA priming followed by recombinant fowl pox virus booster immunizations. This containment did not require neutralizing antibody and was active for a series of challenges ending with a highly virulent virus with a primary isolate envelope heterologous to the immunizing strain.

14) J Virol. 2000 Aug;74(16):7485-95.

Simian immunodeficiency virus (SIV) gag DNA-vaccinated rhesus monkeys develop secondary cytotoxic T-lymphocyte responses and control viral replication after pathogenic SIV infection.

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The potential contribution of a plasmid DNA construct to vaccine-elicited protective immunity was explored in the simian immunodeficiency virus (SIV)/macaque model of AIDS. Making use of soluble major histocompatibility class I/peptide tetramers and peptide-specific killing assays to monitor CD8(+) T-lymphocyte responses to a dominant SIV Gag epitope in genetically selected rhesus monkeys, a codon-optimized SIV gag DNA vaccine construct was shown to elicit a high-frequency SIV-specific cytotoxic T-lymphocyte (CTL) response. This CTL response was demonstrable in both peripheral blood and lymph node lymphocytes. Following an intravenous challenge with the highly pathogenic viral isolate SIVsm E660, these vaccinated monkeys developed a secondary CTL response that arose with more rapid kinetics and reached a higher frequency than did the postchallenge CTL response in control plasmid-vaccinated monkeys. While peak plasma SIV RNA levels were comparable in the experimentally and control-vaccinated monkeys during the period of primary infection, the gag plasmid DNA-vaccinated monkeys demonstrated better containment of viral replication by 50 days following SIV challenge. These findings indicate that a plasmid DNA vaccine can elicit SIV-specific CTL responses in rhesus monkeys, and this vaccine-elicited immunity can facilitate the generation of secondary CTL responses and control of viral replication following a pathogenic SIV challenge. These observations suggest that plasmid DNA may prove a useful component of a human immunodeficiency virus type 1 vaccine.

15) J Virol. 2003 Jul;77(13):7367-75.

Viral escape from dominant simian immunodeficiency virus epitope-specific cytotoxic T lymphocytes in DNA-vaccinated rhesus monkeys.

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Virus-specific cytotoxic T lymphocytes (CTL) are critical for control of human immunodeficiency virus type 1 replication. However, viral escape from CTL recognition can undermine this immune control. Here we demonstrate the high frequency and pattern of viral escape from dominant epitope-specific CTL in SIV gag DNA-vaccinated rhesus monkeys following a heterologous simian immunodeficiency virus (SIV) challenge. DNA-vaccinated monkeys exhibited initial effective control of the SIV challenge, but this early control was lost by serial breakthroughs of viral replication over a 3-year follow-up period. Increases in plasma viral RNA correlated temporally with declines of dominant SIV epitope-specific CD8(+) T-lymphocyte responses and the emergence of viral mutations that escaped recognition by dominant epitope-specific CTL. Viral escape from CTL occurred in a total of seven of nine vaccinated and control monkeys, including three animals that initially controlled viral replication to undetectable levels of plasma viral RNA. These data suggest that CTL exert selective pressure on viral replication and that viral escape from CTL may be a limitation of CTL-based AIDS vaccine strategies.

16) J Virol. 2003 Jan;77(2):1049-58.

Prevention of disease induced by a partially heterologous AIDS virus in rhesus monkeys by using an adjuvanted multicomponent protein vaccine.

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Recombinant protein subunit AIDS vaccines have been based predominantly on the virus envelope protein. Such vaccines elicit neutralizing antibody responses that can provide type-specific sterilizing immunity, but in most cases

do not confer protection against divergent viruses. In this report we demonstrate that a multiantigen subunit protein vaccine was able to prevent the development of disease induced in rhesus monkeys by a partially heterologous AIDS virus. The vaccine was composed of recombinant human immunodeficiency virus type 1 (HIV-1) gp120, NefTat fusion protein, and simian immunodeficiency virus (SIV) Nef formulated in the clinically tested adjuvant AS02A. Upon challenge of genetically unselected rhesus monkeys with the highly pathogenic and partially heterologous SIV/HIV strain SHIV(89.6p) the vaccine was able to reduce virus load and protect the animals from a decline in CD4-positive cells. Furthermore, vaccination prevented the development of AIDS for more than 2.5 years. The combination of the regulatory proteins Nef and Tat together with the structural protein gp120 was required for vaccine efficacy.

17) J Virol. 2002 Jan;76(1):292-302.

ALVAC-SIV-gag-pol-env-based vaccination and macaque major histocompatibility complex class I (A*01) delay simian immunodeficiency virus SIVmac-induced immunodeficiency.

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T-cell-mediated immune effector mechanisms play an important role in the containment of human immunodeficiency virus/simian immunodeficiency virus (HIV/SIV) replication after infection. Both vaccination- and infection-induced T-cell responses are dependent on the host major histocompatibility complex classes I and II (MHC-I and MHC-II) antigens. Here we report that both inherent, host-dependent immune responses to SIVmac251 infection and vaccination-induced immune responses to viral antigens were able to reduce virus replication and/or CD4+ T-cell loss. Both the presence of the MHC-I Mamu-A*01 genotype and vaccination of rhesus macaques with ALVAC-SIV-gag-pol-env (ALVAC-SIV-gpe) contributed to the restriction of SIVmac251 replication during primary infection, preservation of CD4+ T cells, and delayed disease progression following intrarectal challenge exposure of the animals to SIV(mac251 (561)). ALVAC-SIV-gpe immunization induced cytotoxic T-lymphocyte (CTL) responses cumulatively in 67% of the immunized animals. Following viral challenge, a significant secondary virus-specific CD8+ T-cell response was observed in the vaccinated macaques. In the same immunized macaques, a decrease in virus load during primary infection ($P = 0.0078$) and protection from CD4 loss during both acute and chronic phases of infection ($P = 0.0099$ and $P = 0.03$, respectively) were observed. A trend for enhanced survival of the vaccinated macaques was also observed. Neither boosting the ALVAC-SIV-gpe with gp120 immunizations nor administering the vaccine by the combination of mucosal and systemic immunization routes increased significantly the protective effect of the ALVAC-SIV-gpe vaccine. While assessing the role of MHC-I Mamu-A*01 alone in the restriction of viremia following challenge of nonvaccinated animals with other SIV isolates, we observed that the virus load was not significantly lower in Mamu-A*01-positive macaques following intravenous challenge with either SIV(mac251 (561)) or SIV(SME660). However, a significant delay in CD4+ T-cell loss was observed in Mamu-A*01-positive macaques in each group. Of interest, in the case of intravenous or intrarectal challenge with the chimeric SIV/HIV strains SHIV(89.6P) or SHIV(KU2), respectively, MHC-I Mamu-A*01-positive macaques did not significantly restrict primary viremia. The finding of the protective effect of the Mamu-A*01 molecule parallels the protective effect of the B*5701 HLA allele in HIV-1-infected humans and needs to be accounted for in the evaluation of vaccine efficacy against SIV challenge models.

18) J Immunol. 2002 Feb 15;168(4):1847-53.

Recombinant canarypox vaccine-elicited CTL specific for dominant and subdominant simian immunodeficiency virus epitopes in rhesus monkeys.

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Since virus-specific CTL play a central role in containing HIV replication, a candidate AIDS vaccine should generate virus-specific CTL responses. In this study, the ability of a recombinant canarypox virus expressing SIV Gag-Pol-Env (ALVAC/SIV gag-pol-env) was assessed for its ability to elicit both dominant and subdominant epitope-specific CTL responses in rhesus monkeys. Following a series of five immunizations, memory CTL responses specific for a dominant Gag epitope could be demonstrated in the peripheral blood of vaccinated monkeys. Memory CTL responses to a subdominant Pol epitope were undetectable in these animals. Following challenge with SIVmac251, the experimentally vaccinated animals developed high frequency CTL responses specific for the dominant Gag epitope that emerged in temporal association with the early containment of viral replication. Interestingly, the experimentally vaccinated, but not the control vaccinated animals, developed CTL responses to the subdominant Pol epitope that were detectable only after containment of early viremia. Thus, recombinant canarypox vaccination elicited low frequency, but durable memory CTL populations. The temporal association of the emergence of the dominant epitope-specific response with early viral containment following challenge suggests that this immune response played a role in the accelerated clearing of early viremia in these animals. The later emerging CTL response specific for the subdominant epitope may contribute to the control of viral replication in the setting of chronic infection.

19) Vaccine. 2004 Jun 23;22(19):2489-93.

Enhancement of DNA vaccine potency in rhesus macaques by electroporation.

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The potency of an HIV DNA vaccine was enhanced in rhesus macaques by in vivo electroporation, as judged by increased onset, magnitude and duration of antibody and cell-mediated immune responses against both components of a combination Gag and Env vaccine. These data demonstrate the utility of the electroporation technology for use in large animals.

20) J Virol. 2001 Oct;75(19):9037-43.

Induction of potent immune responses by cationic microparticles with adsorbed human immunodeficiency virus DNA vaccines.

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The effectiveness of cationic microparticles with adsorbed DNA at inducing immune responses was investigated in mice, guinea pigs, and rhesus macaques. Plasmid DNA vaccines encoding human immunodeficiency virus (HIV) Gag and Env adsorbed onto the surface of cationic poly(lactide-coglycolide) (PLG) microparticles were shown to be substantially more potent than corresponding naked DNA vaccines. In mice immunized with HIV gag DNA, adsorption onto PLG increased CD8(+) T-cell and antibody responses by approximately 100- and approximately 1,000-fold, respectively. In guinea pigs immunized with HIV env DNA adsorbed onto PLG, antibody responses showed a more rapid onset and achieved markedly higher enzyme-linked immunosorbent assay and neutralizing titers than in animals immunized with naked DNA. Further enhancement of antibody responses was observed in animals vaccinated with PLG/DNA microparticles formulated with aluminum phosphate. The magnitude of anti-Env antibody responses induced by PLG/DNA particles was equivalent to that induced by recombinant gp120 protein formulated with a strong adjuvant, MF-59. In guinea pigs immunized with a combination vaccine containing HIV env and HIV gag DNA plasmids on PLG microparticles, substantially superior antibody responses were induced against both components, as measured by onset, duration, and titer. Furthermore, PLG formulation overcame an apparent hyporesponsiveness of the env DNA component in the combination vaccine. Finally, preliminary data in

rhesus macaques demonstrated a substantial enhancement of immune responses afforded by PLG/DNA. Therefore, formulation of DNA vaccines by adsorption onto PLG microparticles is a powerful means of increasing vaccine potency.

21) J Virol. 1999 Oct;73(10):8201-15.

Role of immune responses against the envelope and the core antigens of simian immunodeficiency virus SIVmne in protection against homologous cloned and uncloned virus challenge in Macaques.

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We previously showed that envelope (gp160)-based vaccines, used in a live recombinant virus priming and subunit protein boosting regimen, protected macaques against intravenous and intrarectal challenges with the homologous simian immunodeficiency virus SIVmne clone E11S. However, the breadth of protection appears to be limited, since the vaccines were only partially effective against intravenous challenge by the uncloned SIVmne. To examine factors that could affect the breadth and the efficacy of this immunization approach, we studied (i) the effect of priming by recombinant vaccinia virus; (ii) the role of surface antigen gp130; and (iii) the role of core antigens (Gag and Pol) in eliciting protective immunity. Results indicate that (i) priming with recombinant vaccinia virus was more effective than subunit antigen in eliciting protective responses; (ii) while both gp130 and gp160 elicited similar levels of SIV-specific antibodies, gp130 was not as effective as gp160 in protection, indicating a possible role for the transmembrane protein in presenting functionally important epitopes; and (iii) although animals immunized with core antigens failed to generate any neutralizing antibody and were infected upon challenge, their virus load was 50- to 100-fold lower than that of the controls, suggesting the importance of cellular immunity or other core-specific immune responses in controlling acute infection. Complete protection against intravenous infection by the pathogenic uncloned SIVmne was achieved by immunization with both the envelope and the core antigens. These results indicate that immune responses to both antigens may contribute to protection and thus argue for the inclusion of multiple antigens in recombinant vaccine designs.

22) J Virol. 1999 Apr;73(4):3134-46.

Protection of macaques against intrarectal infection by a combination immunization regimen with recombinant simian immunodeficiency virus SIVmne gp160 vaccines.

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We previously reported that immunization with recombinant simian immunodeficiency virus SIVmne envelope (gp160) vaccines protected macaques against intravenous challenge by the cloned homologous virus E11S but that this protection was only partially effective against the uncloned virus, SIVmne. In the present study, we examine the protective efficacy of this immunization regimen against infection by a mucosal route. We found that the same gp160-based vaccines were highly effective against intrarectal infection not only with the E11S clone but also with the uncloned SIVmne. Protection against mucosal infection is therefore achievable by parenteral immunization with recombinant envelope vaccines. Protection appears to correlate with high levels of SIV-specific antibodies and, in animals protected against the uncloned virus, the presence of serum-neutralizing activities. To understand the basis for the differential efficacies against the uncloned virus by the intravenous versus the intrarectal routes, we examined viral sequences recovered from the peripheral blood mononuclear cells of animals early after infection by both routes. We previously showed that the majority (85%) of the uncloned SIVmne challenge stock contained V1 sequences homologous to the molecular clone from which the vaccines were made (E11S type), with the remainder

(15%) containing multiple conserved changes (the variant types). In contrast to intravenously infected animals, from which either E11S-type or the variant type V1 sequences could be recovered in significant proportions, animals infected intrarectally had predominantly E11S-type sequences. Preferential transmission or amplification of the E11S-type viruses may therefore account in part for the enhanced efficacy of the recombinant gp160 vaccines against the uncloned virus challenge by the intrarectal route compared with the intravenous route.

23) J Virol. 1999 Jan;73(1):618-30.

Limited breadth of the protective immunity elicited by simian immunodeficiency virus SIVmne gp160 vaccines in a combination immunization regimen.

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We previously reported that immunization with recombinant simian immunodeficiency virus SIVmne envelope (gp160) vaccines protected macaques against an intravenous challenge by the cloned homologous virus, E11S. In this study, we confirmed this observation and found that the vaccines were effective not only against virus grown on human T-cell lines but also against virus grown on macaque peripheral blood mononuclear cells (PBMC). The breadth of protection, however, was limited. In three experiments, 3 of 10 animals challenged with the parental uncloned SIVmne were completely protected. Of the remaining animals, three were transiently virus positive and four were persistently positive after challenge, as were 10 nonimmunized control animals. Protection was not correlated with levels of serum-neutralizing antibodies against the homologous SIVmne or a related virus, SIVmac251. To gain further insight into the protective mechanism, we analyzed nucleotide sequences in the envelope region of the uncloned challenge virus and compared them with those present in the PBMC of infected animals. The majority (85%) of the uncloned challenge virus was homologous to the molecular clone from which the vaccines were made (E11S type). The remaining 15% contained conserved changes in the V1 region (variant types). Control animals infected with this uncloned virus had different proportions of the two genotypes, whereas three of four immunized but persistently infected animals had >99% of the variant types early after infection. These results indicate that the protective immunity elicited by recombinant gp160 vaccines is restricted primarily to the homologous virus and suggest the possibility that immune responses directed to the V1 region of the envelope protein play a role in protection.

24) Science. 1992 Jan 24;255(5043):456-9.

Protection of macaques against SIV infection by subunit vaccines of SIV envelope glycoprotein gp160.

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Simian immunodeficiency virus (SIV) is a primate lentivirus related to human immunodeficiency viruses and is an etiologic agent for acquired immunodeficiency syndrome (AIDS)-like diseases in macaques. To date, only inactivated whole virus vaccines have been shown to protect macaques against SIV infection. Protective immunity was elicited by recombinant subunit vaccines. Four Macaca fascicularis were immunized with recombinant vaccinia virus expressing SIVmne gp160 and were boosted with gp160 produced in baculovirus-infected cells. All four animals were protected against an intravenous challenge of the homologous virus at one to nine animal-infectious doses. These results indicate that immunization with viral envelope antigens alone is sufficient to elicit protective immunity against a primate immunodeficiency virus. The combination immunization regimen, similar to one now being evaluated in humans as candidate human immunodeficiency virus (HIV)-1 vaccines, appears to be an effective way to elicit such immune responses