

Madison, Wilton

18-01657-E

From: Mark Edwards <medwards@biosciadvisors.com>
Sent: Monday, January 01, 2018 8:35 PM
To: foiapa
Subject: FOIA Request

RECEIVED

JAN 02 2018

Office of
FOIA Services

I would like to request access to Exhibit 10.1 to the 9/30/07 10-Q, filed by GenVec, Inc. on 11/9/2007. Confidential treatment was sought as to certain portions when initially filed with the Commission.

In the event that confidential treatment has not expired or has been extended, I further request that you send me the expiration date(s) from the relevant CT order(s) so I will know when I should resubmit my request.

I authorize up to \$61 in search and retrieval fees. Please send the exhibit(s) by PDF if possible.

Sincerely,

Mark

Mark G Edwards
Managing Director
Bioscience Advisors
2855 Mitchell Dr., Suite 103
Walnut Creek, CA 94598
medwards@biosciadvisors.com
925 954-1397



UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
STATION PLACE
100 F STREET, NE
WASHINGTON, DC 20549-2465

Office of FOIA Services

February 15, 2018

Mr. Mark G. Edwards
Bioscience Advisors
2855 Mitchell Dr., Suite 103
Walnut Creek, CA 94598

RE: Freedom of Information Act (FOIA), 5 U.S.C. § 552
Request No. 18-01657-E

Dear Mr. Edwards:

This letter is in response to your request, dated January 01, 2018 and received in this office on January 02, 2018, for access to Exhibit 10.1, to the September 30, 2007 Form 10-Q, filed by GenVec, Inc. on November 9, 2007.

The search for responsive records has resulted in the retrieval of the above-requested exhibit, totaling 23 pages of records that may be responsive to your request. They are being provided to you with this letter.

If you have any questions, please contact me at wadeo@sec.gov or (202) 551-8323. You may also contact me at foiapa@sec.gov or (202) 551-7900. You also have the right to seek assistance from Ray J. McInerney as a FOIA Public Liaison or contact the Office of Government Information Services (OGIS) for dispute resolution services. OGIS can be reached at 1-877-684-6448 or Archives.gov or via e-mail at ogis@nara.gov.

Sincerely,

A handwritten signature in black ink that reads "Ollie R. Wade".

Ollie R. Wade
FOIA Research Specialist

Enclosures

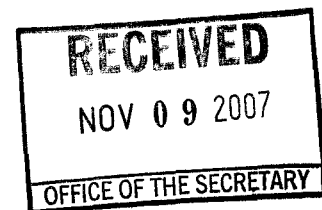
Other Transactions (OT) Agreement/Modification P00001
OTHER TRANSACTION FOR PROTOTYPE AGREEMENT

BETWEEN

GenVec, Inc.
 65 West Watkins Mill Road
 Gaithersburg, MD 20878

AND

The Department of Homeland Security
 Science & Technology Directorate
 Washington, DC 20528



Agreement Number: HSHQDC-07-9-00004
 Modification Number: P00001
 Concerning Human Adenovirus Type C, Serotype 5
 Replication Deficient Foot-and-Mouth Disease (FMD) Serotype-Specific Vectors,
 Vaccines, and Vectored Biological Immunomodulators

Base Period:

Total Value of Base Period: \$5,976,726
 GenVec's Cost Share/Contribution: \$0.00
 Government's Cost Share/Contribution: \$5,976,726
 Funds Obligated: \$5,976,726

Option 1:

Total Value of Option 1: \$5,613,815
 GenVec's Cost Share/Contribution: \$0.00
 Government's Cost Share/Contribution: \$5,613,815
 Funds Obligated: \$5,613,815
 PR Number: RSCB-07-00200
 Line of Accounting: NONE000-000-7X-31-01-0 1-002-01-00-
 0000-00-00-00-0 0-GE-OE-25-11-000000

Authority: Section 831 of the Homeland Security Act of 2002, Public Law 107-296
 The Modification of the Agreement is entered into between the United States of America,
 hereinafter called the Government, represented by The Department of Homeland
 Security (DHS), and GenVec, Inc., pursuant to and under US Federal law.

FOR GenVec:

FOR DHS:

GenVec/Date

OT Agreements Officer/Date

AUG 30 2007

The following articles are revised as follows:

ARTICLE II: TERM is amended to add the following:

The period of performance of Option 1 of this agreements starts on date of award and ends on 31 January 2008.

ARTICLE III: STATEMENT OF OBJECTIVES is revised to incorporate the following tasks for Option 1:

I. Background

The Department of Homeland Security (DHS) is committed to using cutting edge technologies and scientific talent in its quest to make America safer. DHS's Directorate of Science & Technology (S&T) is tasked with researching and organizing the scientific, engineering, and technological resources of the United States and leveraging these existing resources into technological tools to help protect the homeland. In support of this effort, the DHS S&T Plum Island Animal Disease Center (PIADC) in Long Island, NY, is a unique research facility and critical national asset conducting research on diseases of livestock to protect America from terrorist threats directed against agriculture from the intentional introduction of diseases. As defined in Homeland Security Presidential Directive-7 (HSPD-7) and HSPD-9, the Secretary of Homeland Security is responsible for coordinating the overall national effort to enhance the protection of the critical infrastructure and key resources of the United States, including the defense of agriculture and food. To fulfill these requirements, DHS S&T supports programs at PIADC to strengthen the nation's ability to predict and respond to the incursion of a foreign animal disease.

DHS S&T requires scientific, vaccine development and regulatory services from GenVec, Inc. (GenVec). GenVec is a non-traditional contractor that has core competencies in patent protected technology platforms for replication-defective recombinant adenovirus serotype 5(rAd5) based-vaccines and therapeutic product candidates. GenVec's technology has been successfully applied to discovery, pre-clinical, and clinical (Phase I-II) trials for human vaccines. GenVec also has experience in Ad5 production (scale-up and downstream processing) with an integrated QA program.

GenVec has held a historical contractual scientific relationship with the USDA ARS on a Foot-and-Mouth Disease Virus (FMDV) countermeasure R&D program. Specifically, USDA and GenVec entered into Specific Cooperative Agreements (SCAs) in 2004-2005 and 2005-2006 to use reasonable commercial efforts to construct, produce and test a rAd5 based vector containing FMDV serotype empty capsids as part of a Plum Island FMD vaccine and immunomodulator program. These SCAs were funded through DHS-USDA interagency agreements and DHS S&T scientists have been involved in the testing and evaluation of several rAd5 based vaccine vectors since 2005. In addition, USDA and GenVec have been interacting through a Collaborative Research and Development

Agreement (CRADA) since 2004. The objective of the CRADA is to jointly construct and test GenVec Advectors expressing FMD genes and livestock cytokines, and to identify Advectors and complementing cell lines that have the potential to serve as a viral-vectored platform for a new generation of FMD vaccines. DHS S&T scientists have participated in the USDA-GenVec CRADA since 2004 through a DHS-USDA ARS interagency agreement on the joint research and development of FMD countermeasures, such as FMD vaccines and biological immunomodulators.

Based on the successful technical outcome to date of the base year contract agreement (awarded 1 February 2007) and the initiation and acceleration of pre-product development activities at GenVec (originally targeted for option year 1) that has resulted in the acceleration of lead FMD vaccine material for testing, DHS would like to move forward with GenVec and exercise option year 1 to allow uninterrupted continuation and development of the lead FMD vaccine candidate for eventual licensing by USDA Center for Veterinary Biologics. These products would be made available for potential manufacture and procurement by the USDA National Center for Animal Health Emergency Management National Veterinary Stockpile to help accomplish critical mission objectives with regard to live FMDV and vaccine countermeasures against high consequence Foreign Animal Diseases such as those caused by FMDV.

II. Scope of Work

For option year 1, milestone 1 **has been revised to add the following work activities:**

- 1. Complete Construction and Testing of Additional (New) Ad5-FMD Serotype Vaccine Vectors.**
- 2. Initiate in vitro assay development studies centered on in vitro potency.**
- 3. Initiate analytical and biochemical studies focused on vaccine potency improvements**

For option year 1, **work activities for milestones 2 and 3 from the original SOW remain unchanged.**

For option year 1, milestones 4 and 5 **have no work activity (not funded).**

For option year 1, milestone 6 **from the original SOW remains unchanged.**

For option year 1, milestone 7 **has been revised to add the following work activities.**

- 1. Conduct 10L bioreactor upstream and downstream optimization studies in advance of full development process development work for technology transfer to manufacturing. Provide material to DHS for animal safety and efficacy testing.**

III. Deliverables.

See Attachment II for detailed list and description of technical data and physical deliverables associated with each of the two revised milestones (milestones 1 and 7).

IV. Other Contract Details

A. **Period of Performance.** The period of performance for this revised SOW is a base period from the contract year one option award date to January 31, 2008, with the option to negotiate and award an additional one (1) one-year period. DHS may give subsequent extension notices to GenVec, Inc. in writing for further performance in accordance with the terms of this SOW.

B. **Travel.** All travel must be approved by the DHS Technical Representative. All foreign travel must be approved in advance by the ORD Program Manager, DHS Programs, Plans and Budgets (PPB), and the DHS S&T Special Assistant for International Policy.

C. DHS-Furnished Information.

- i. DHS will provide certain DHS information, materials, and forms unique to DHS to GenVec, Inc. to support certain tasks under this SOW. Delays in the supply of DHS information, materials to GenVec could result in delays to the completion of certain deliverables.
- ii. The DHS S&T Technical Representative identified in this SOW will be the point of contact (POC) for identification of any required information to be supplied by DHS.
- iii. GenVec, Inc. will prepare any documentation according to the guidelines provided by DHS.

D. **Place of Performance.** GenVec, Inc. will perform the work under this SOW at their place of R&D business, located in Gaithersburg, MD and through the use of sub-contractors where required as identified in this SOW.

E. **DHS-Furnished Property.** DHS property will not be provided to GenVec, Inc. unless otherwise agreed to by the parties of the agreement.

F. **Deliverables.** GenVec, Inc. will provide all deliverables identified in this SOW directly to the DHS S&T Technical Representative with a copy of the transmittal letter to the Other Transaction Contracting Officer and as otherwise specified in this SOW.

- H. **Publications.** All manuscripts must be approved prior to submission by the DHS S&T Technical Representative at PIADC and by the GenVec Technical Representative with approval not to be unreasonably withheld by either party.
- I. **Program Status Report.** GenVec, Inc. will deliver a quarterly program status reports to the DHS S&T Technical Representative and DHS S&T Resource Manager containing the following metrics: (1) monthly scientific reports will be delivered to the DHS S&T Technical Representative according to mutually agreed upon format and content requirements; and (2) a monthly report, including financial, schedule, and scope information, risk information and an assessment of performance will be delivered to the DHS S&T Technical Representative and the DHS S&T Resource Manager. Financial data should include monthly expenditures for labor, travel and equipment.
- J. **Security Requirements.** All work performed under this SOW is unclassified unless otherwise specified by DHS. If classified work is required under this SOW, DHS will provide specific guidance to the contractor as to which work will be conducted in a classified manner and at which classification level. GenVec, Inc. participants will also adhere to applicable government orders, guides, and directives while performing the work hereunder.

V. Points of Contact

GenVec, Inc. Points of Contact (POCs) are as follows:

- Technical POC(s) –
Doug Brough, PhD, Senior Director, Vector Services
65 West Watkins Road
Gaithersburg, MD 20878
Phone : **240-632-5540**
dbrough@genvec.com
- Financial POC(s) –
Bill Enright
65 West Watkins Road
Gaithersburg, MD 20878
Phone: **301-944-1183**
benright@genvec.com

The DHS POCs are as follows:

- DHS S&T Technical Representative –

Dr. Tam Garland
Ag Program Manager

Department of Homeland Security
ATTN: Science and Technology Directorate
Washington, DC 20528
(202) 254-6885
tam.garland@dhs.gov

- Resource Manager

Scott Randels
Department of Homeland Security
ATTN: Science and Technology Directorate/*Office, Mr. Scott Randels*
Washington, DC 20528
(202) 254-6053
Scott.randels@dhs.gov

Either party may change its representatives named in this Statement of Work by written notification to the other Party. The Government will effect the change as stated in subparagraph C.4 of Article IV of the Other Transaction Agreement.

ATTACHMENT 1 – STATEMENT OF WORK EXECUTION (Option Year 1)

Milestone 1: Complete Construction and Testing of Additional Ad5-FMD Serotype Vaccine Vectors Using Different FMD Capsid Promoters, FMD Capsid Genes and FMD Protease Genes (new funded activity, Option Year 1).

General Approach

To accomplish the new activities required under revised Milestone 1, GenVec will use commercially reasonable efforts to complete construction and testing of additional Ad5-FMD serotype vaccine vectors, GenVec will leverage its existing technology (as described below) for adenoviral vector construction, testing, production, storage and shipping in order to rapidly and efficiently advance the FMDV genes into Adenovectors suitable for pre-clinical experiments and toxicology testing, as well as to support cGMP material production. GenVec's Vector Core, Vector Sciences, Preclinical Sciences, Quality Assurance, Regulatory Affairs, Quality Control and Analytical Sciences R&D departments have a proven track record for the successful construction, production and testing of Adenovectors - having performed this activity for many hundreds of Adenovectors for research and development.

To meet the new requirements of revised Milestone 1 GenVec will use commercially reasonable efforts to prepare toxicology stocks and, from these, advance selected vectors to GMP manufacturing), GenVec will utilize its rapid vector construction system (designated AdFAST™) to produce its adenoviral vector (designated "GV11") and its proprietary cell line (designated "293-ORF6" and "M2A") that will yield adenoviral vectors that are replication deficient and eliminate the potential for replication competent adenovirus (RCA) arising as a result of homologous recombination. This technology is important to vaccine development, as the presence of RCA in lots of Adenovector raises a variety of safety concerns, including the possibility of adenovirus infection, unintended vector replication due to the presence of wild-type helper function, and exacerbation of host inflammatory responses [see - Guidance for Industry: Guidance for Human Somatic Cell Therapy and Gene Therapy, FDA, March 1998]. The GV11 vector provides ~2 kb more capacity for modified forms of FMDV genes. This vector construct does not express any adenoviral E4 genes, which may provide advantages for use as a vaccine, as the deletion of the E4 region has the potential to reduce the number of viral genes in the vector and may reduce potential safety concerns. GenVec's use of cell line (M2A) and vector system also provides risk reduction during construction as well as production of Adenovectors that express transgene products (antigens) that interfere with adenovirus growth in tissue culture or that are cytotoxic. During the course of its previous work with ARS and DHS, GenVec has shown that this system is important for the further development of FMDV expressing Adenovectors.

GenVec's in-house activities will include commercially reasonable efforts for Adenovector construction, production, and testing of pre-clinical Adenovectors that can be used for pre-clinical experiments and toxicology studies as well as providing materials

for cGMP production. The internally generated documentation to support construction and production of each of the Adenovector products will be reviewed for accuracy and completeness by GenVec's in-house Quality and Analytical Sciences department. GenVec will base the characterization (*i.e.*, all testing) for all cGMP materials (*i.e.*, cell banks, virus banks, clinical materials) upon either direct communications with regulatory agencies (*e.g.*, FDA, USDA, CVB) or published regulatory guidance documents. GenVec will hold a Pre-SIF meeting with the USDA/CVB/DHS.

Adenovector Construction

GenVec has developed AdFAST™, a system for the rapid construction of high quality adenoviral vectors that will be critical in meeting the needs of the project. A flow diagram of this process is depicted in Figure 1. The following summarizes the vector construction, vector expansion and clinical seed stock (CSS) processes.

The GV11 adenoviral vector (Adenovector) contains an expression cassette that replaces the E1 region of the vector, with additional deletions of a portion of the E3 region and the entire E4 region. Additionally, the GV11 Adenovector contains a transcriptionally inert spacer (TIS1) sequence in the deleted E4 region, as E4-deleted Adenovectors without a spacer typically have comparatively poor growth characteristics. For the purposes of this proposal, GenVec will depict construction with a CMV promoter. As noted FMDV transgenes will be expressed from alternative promoters and will be evaluated by GenVec for their ability to be produced in this configuration in GenVec's GV11/293-ORF6 system or GenVec's GV11/M2A system. [Note: GenVec has secured a license for use of the CMV promoter from the University of Iowa] There are a number of options available for the construction of such vectors (*e.g.*, alternate promoters, expression cassette configurations) and GenVec has extensive experience constructing Adenovectors with these expression cassette variations to optimize transgene expression and Adenovector growth. For the purposes of this proposal beyond milestone 1 GenVec will assume the Ad5-FMD Adenovector is utilizing the CMV promoter to drive expression and the vector configuration shown.

The complementing cell line used to grow GV11 Adenovectors is designated as 293-ORF6 or M2A. The 293-ORF6 cell line was derived from 293 cells obtained from the ATCC (CRL-1573) [Note: The 293 cell line is a permanent line of primary human embryonal kidney transformed by sheared human adenovirus type 5 (Ad 5) DNA]. The 293-ORF6 cell line functionally complements for the E1 and E4 regions missing from the GV11 vector to allow for vector production. These 293-ORF6 cells were constructed by stably transforming 293 cells with an inducible E4-ORF6 expression cassette. See "293-ORF6 Cell Line" below for further details regarding the construction of the 293-ORF6 cells and cell line thereof.

The M2A cells were constructed by stably transforming 293-ORF6 cells with a constitutive TetReceptor expression cassette. See "M2A" cell line banking for further details. M2A and 293-ORF6 cells can be used for construction of Adenovectors and the

process is identical. For the purposes of describing the construction process 293-ORF6 cells will be used as the production cell line.

The construction process will begin with the isolation of the FMDV genes in appropriate plasmid fragments. Each fragment will be recombined in *E. coli* BJ1q bacteria with the GV11 vector base AdFAST™ plasmid pAdE1(BN)E3(10)E4(TIS1). Positive clones will be identified by restriction enzyme analysis of miniprep DNA. A single clone will be chosen and a large preparation of plasmid DNA will be produced and purified by the Endofree Plasmid Maxi Kit procedure from Qiagen. The resulting plasmid preparation will be confirmed by restriction endonuclease digestion. A depiction of the procedure used in cloning and synthesis and construction of a typical GV11 vector, along with typical base and intermediate plasmid diagrams, is included in Figure 1. A graphic map of a typical AdFAST™ Plasmid intermediate is presented in Figure 2. [Note: the gene of interest is designated as "GeneX".]

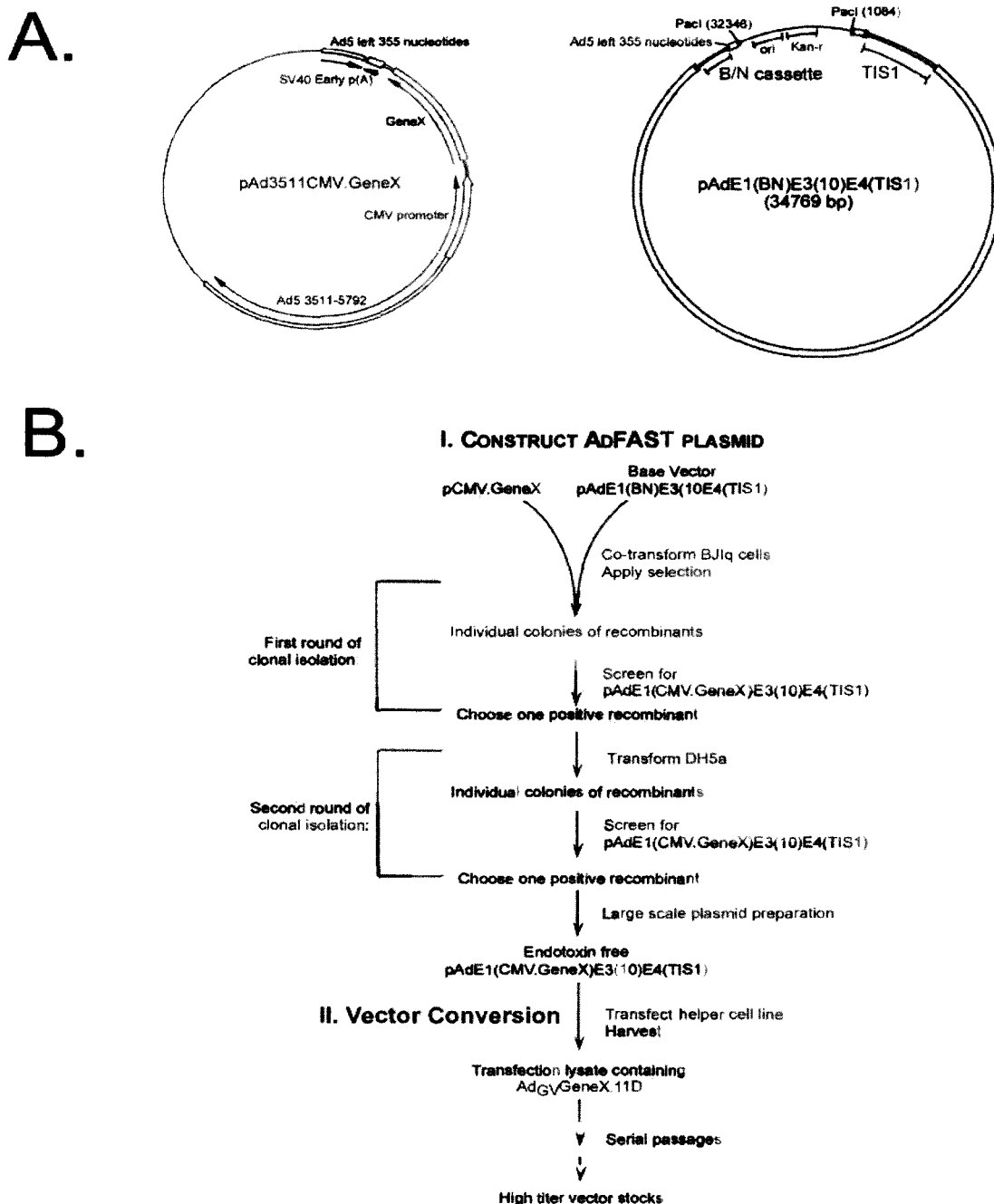


Figure 1 – Construction of AdGVGeneX.11D by the AdFAST™ method. A. Plasmids are recombined to generate pAdE1(CMV.GeneX)E3(10)E4(TIS1). The donor plasmid, pCMV-GeneX, contains the GeneX expression cassette flanked by adenovirus sequence homologous to the adenovirus sequence flanking the BN cassette in the base vector, pAdE1(BN)E3(10)E4(TIS1). A double homologous recombination event between the two plasmids will replace the bacteriostatic BN cassette with the GeneX expression cassette.

B. Flow chart of vector construction by the AdFAST™ method.

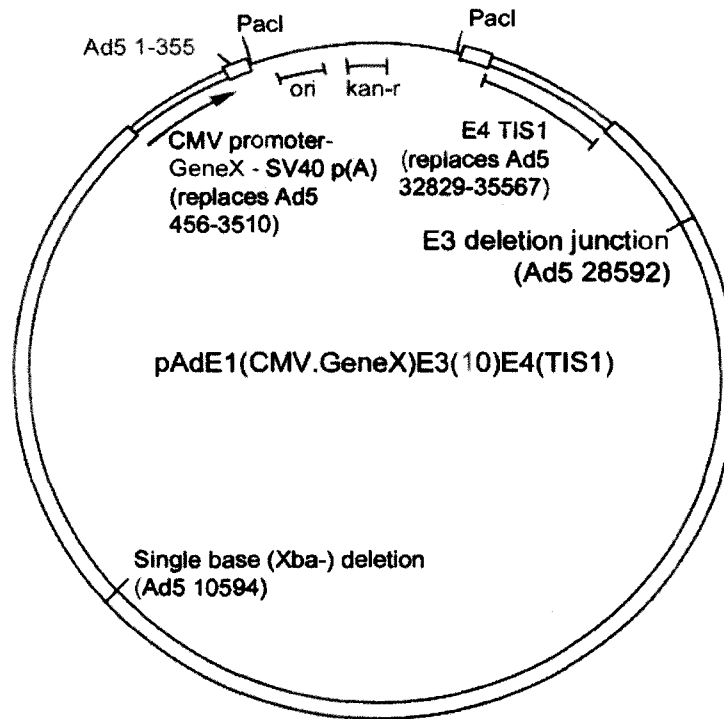


Figure 2 – Graphic map of the AdFAST™ Plasmid pAdE1(CMV.GeneX)E3(10)E4(TIS1).

To complete the vector construction, the AdFAST™ plasmid will be linearized with PacI and transfected using standard procedures in the 293-ORF6 cell line. The Adenovector in lysate from transfected cells will be serially passaged to expand the titer of Adenovector. The identity and integrity of the passages will be verified by PCR and this material will be used to generate the Vector Seed Stock (VSS) stored at $\leq -60^{\circ}\text{C}$ to -95°C .

The resulting Adenovector (AdGVGeneX.11D) will contain the CMV.GeneX expression cassette that replaces the deleted adenovirus E1 region. Other adenovirus regions deleted will include a partial E3, and all of E4 (the E4 region has been replaced with a transcriptionally inert spacer element – TIS1). Figure 3 provides a representative view of these regions in comparison with wild type Ad5.

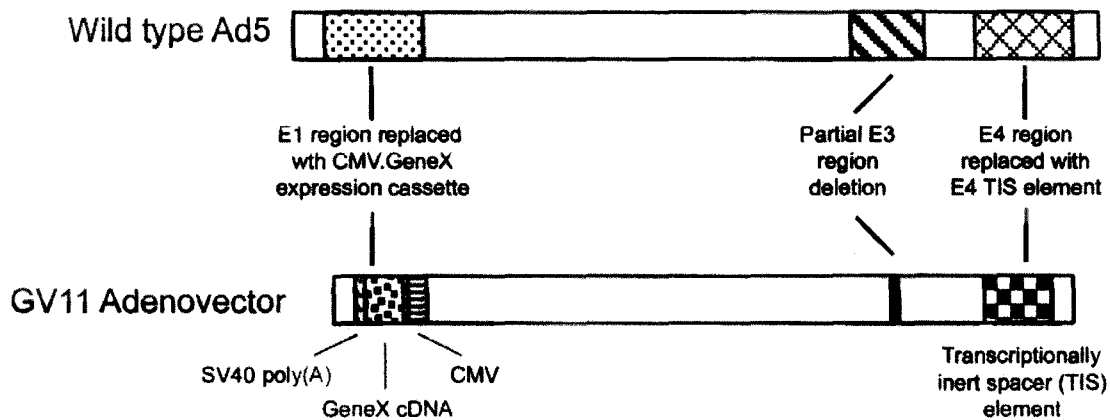


Figure 3 – A graphical depiction of wild type adenovirus type 5 (Ad5) and a GV11 Adenovector demonstrating the E1, E4, and partial E3 deletions and the structure of the expression cassette that includes the GeneX cDNA, the CMV promoter and the SV40 poly A stop sequences. Inclusion of the transcriptionally inert spacer (TIS) element increases the yield of purified virus.

The flow diagram in Figure 4 provides a description of the estimated vector expansion steps (following initial construction of the Adenovector) to generate the Vector Seed Stock and the testing performed at each stage. Note that for each step leading up to the Vector Seed Stock, cells from the existing 293-ORF6 MWCB L/N: 2003-0039 will be used. These cells are adherent cells that utilize porcine trypsin and fetal bovine serum for passaging and culture. Any porcine trypsin and Fetal Bovine Serum (FBS) used in any of the processes described herein are obtained only from BSE free sources in the United States and GenVec will maintain the Certificates of Analysis on file. Furthermore, the absence of adventitious bovine and porcine viruses will be confirmed prior to release of both the Master Cell Bank and Manufacturer's Working Cell Bank.

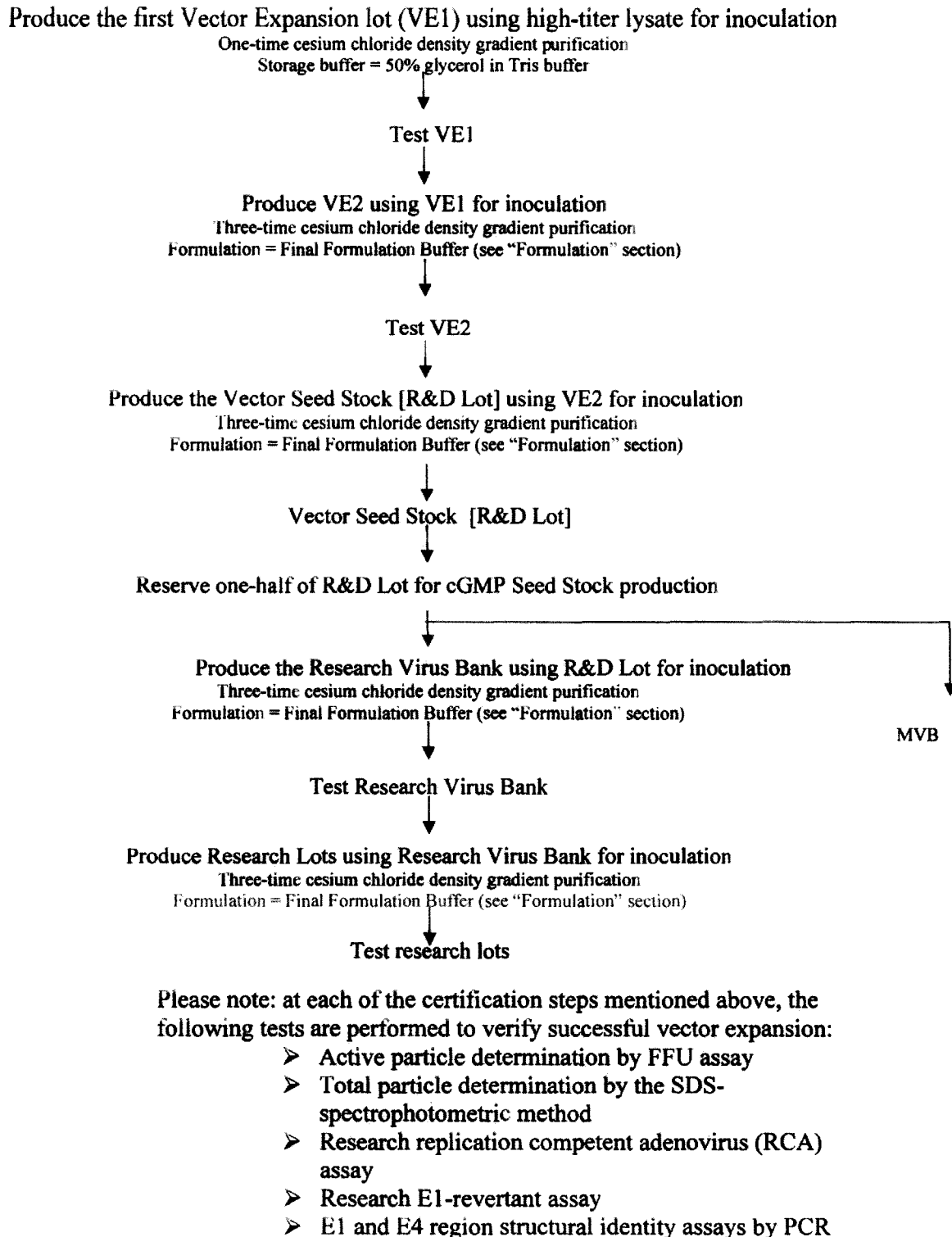


Figure 4: Vector Expansion and Vector Seed Stock [R&D Lot] Establishment

As indicated in Figure 4 above, the R&D Lot will be divided into two parts – one part will be used to generate a Research Virus Bank for the purposes of generating research lots and the other part will be used to produce the Master Virus Bank.

Based upon GenVec's experience with Adenovector product development, GenVec will use commercially reasonable efforts to produce research lots from expansions of the Research Virus Bank to allow sufficient materials to perform assay development work as well as to plan for additional *in vitro* and *in vivo* evaluations. Therefore, each of the Adenovectors built will include research production lots of approximately 10^{12} viral particle units. Please note, because each specific transgene may affect vector production (*i.e.*, yield), the production numbers above are approximations, as indicated, while these estimates are based upon its significant experience, the yield must be confirmed once the Adenovectors have been constructed and have gone through some preliminary productivity experiments. Because of these potential issues for Ad5-FMD and its experiences with these constructs, GenVec has included the banking and use of its M2A cell line in milestones 3 and 4, which will lower these risks to the development of adenovirus, vectored molecular vaccines for FMDV.

Please note that in order to confirm transgene expression during the course of conducting activities under revised Milestone 1, GenVec may rely upon DHS at Plum Island for assessing this function until such time that GenVec has established such an assay for each FMDV Adenovector. These assays are critical for the further development of Ad5-FMD and therefore, the current team (GenVec, DHS, USDA ARS) approach to developing expression assays is crucial to meeting the timeline for this SOW.

Sequencing to Confirm Construction

Sequencing of the genome will occur at three stages – 1) sequencing of all of the cDNA inserts will occur early in vector construction; 2) sequencing of the remaining non-native adenovirus regions in the AdFAST plasmid upon successful vector construction; 3) sequencing of the first cGMP production lot for the FMD Adenovector. Prior to initial lot release of the cGMP production of the FMD Adenovector, all 3 sequences should be within specifications and as expected.

Description of FMD Adenoviral Vaccine Vectors

GenVec intends to provide Adenovectors engineered and constructed using GenVec's proprietary vector construction technology. The revised option year 1 work will add additional Adenovectors to the program that could provide additional vaccine candidates to the development pipeline and eventual cGMP manufacture. The specific Adenovectors to be added will be done in consultation with DHS and will be selected from the one or more of the following FMDV serotypes: A, O, Asia, SAT1, SAT2, and SAT3..

cGMP Vector Seed Stock (R&D Lot) Production and Characterization

The testing of a R&D Lot is as per Table 2 below and all resulting lots must meet specifications prior to use in a production of a vaccine candidate vector.

Table 2: cGMP Vector Seed Stock (R&D Lot) Testing

Cell Harvest	
ASSAY NAME	SPECIFICATION
Test for the Presence of Agar-Cultivable and Non-Agar Cultivable Mycoplasma for Adenovirus Samples	No Growth
Purified Bulk Samples	
ASSAY NAME	SPECIFICATION
Test for the Presence of Bacterial and Fungal Contaminants: Sterility Using a Direct Inoculation Method	No Growth
Particle Number Determination (PU)	Report Result
Focus Forming Unit Assay Procedure (FFU Titer)	Report Result
PU/FFU Ratio	< 30 PU/FFU
Demonstration of Transgene Expression Using Western Blotting Technique	Pass
Replication Competent Adenovirus	None Detected
Genetic Structural Identity	Pass
E1-Revertant Assay	Report Result

Note: The nature of the testing program is subject to change pending CVB meeting/review

In Vitro Potency Assay Development Studies (New Funding Activity Option year 1)

A new activity in Milestone 1 (funded by option year 1) is to “Initiate *in vitro* assay development studies centered on *in vitro* potency”. To do this GenVec will involve a team of scientists with expertise in assay development. Scientists with expertise in assay development will evaluate and explore *in vitro* methods to detect and quantitate Adenovector FMDV proteins. Areas of immediate discussion and exploration include purification of Ad5-FMD antigen from M2A infected cells, production and characterization of antibody reagents to FMDV proteins, development and pre-validation of *in vitro* quantitative assays, and qualification of reagents. It is expected that any new assay that is developed here would be incorporated into the later development of the project at some future time before large-scale production for stockpiling or commercialization.

Analytical and Biochemical Vaccine Potency Studies (New Funding Activity Option Year 1)

An additional activity in Milestone 1 is to “Initiate analytical and biochemical studies focused on vaccine potency improvements”. To do this GenVec will continue to involve a team of scientists with expertise in its process and in Adenovector biochemistry to our existing collaboration team structure with DHS, USDA ARS and GenVec. Scientists with expertise in the research and development of FMD will evaluate and explore process alternatives and modifications that DHS agrees will be critical to steps to reach the stockpiling of Ad5-FMD vaccines. Areas of immediate discussion and exploration include the purification and characterization of large (>500,000 kDa MW; >10nm) FMDV antigen complexes present during downstream processing, efforts to determine if these complexes contribute to overall vaccine potency, and if so, determination if modifications of existing upstream and downstream processes can be optimized to increase the production of these FMDV complexes to improve overall vaccine potency. It is expected that any modification to the manufacturing process that is explored here would be incorporated into the later development of the project at some future time before large-scale production for stockpiling or commercialization.

Milestone 7 – Production of Clinical Lot for Animal Studies (Option Year 1)

The purpose of this milestone is to generate a sufficient quantity of FMD vaccine candidate vials using commercially reasonable efforts and GenVec’s advanced scalable manufacturing process (bioreactor production with column chromatography purification, further described below) for critical approval animal studies that GenVec will conduct with DHS in Milestone 8. Completion of this milestone will position the program for successful future large-scale production of vaccine for stockpiling and commercialization. Until recently (March 2007), research lots of FMD vector candidates for DHS testing and evaluation have been produced using GenVec’s base manufacturing process that enables rapid entry of vector candidates into animal studies for evaluation of safety and efficacy at a relatively small scale. While efficient and cost effective for conducting lead molecule evaluation, this process lacks the potential for significant scale-up at several key process steps due to the labor-intensive nature of the base process (see process comparison, Table 9 below) and can be subject to significant process variability when attempting large-scale production.

Table 9: **Process Comparison**

Production Step	Base Process	Advanced Scalable Process
Cell Culture	Serum-free suspension culture of production cells in multiple 1 L shaker flasks (1 to 48 L)	Serum-free suspension of production cells in stirred tank bioreactor (scalable from 1 L to 10,000 L)
Infection	Addition of virus bank and ZnCl (to induce E4 express) to individual shaker flasks	Addition of virus bank and ZnCl to single bioreactor using a closed system pump

Cell Lysis	3 Freeze/thaw cycles of centrifuged cell pellets	Detergent lysis within bioreactor by addition of Triton X-100)
Initial Processing	Benzonase digestion and Freon extraction	Ultrafiltration, Benzonase digestion and diafiltration within closed system
Purification	3 cycles of density gradient centrifugation on CsCl	Column chromatography
Buffer Exchange	Dialysis into final formulation buffer	Size exclusion chromatography into final formulation buffer

For GenVec's vaccine and therapeutic programs, the overall strategy has been to rapidly generate relatively small scale clinical vector stocks using the base process for initial clinical assessment and then to employ the advanced, scalable process for pivotal, Phase III or proof-of-concept clinical trials. This approach has been successfully employed for both the AdHIV vaccine program, in collaboration with the Vaccine Research Center of NIAID and for the TNFerade program for cancer therapy.

For Milestone 7, GenVec will convert the manufacturing process for the FMD vaccine candidate vector over to the advanced scalable manufacturing process in GenVec's Process Development laboratories and then transfer this process to a contract manufacturing facility (Molecular Medicine, Carlsbad, CA) for production of Ad5-FMD vaccine lots under cGMP conditions.

Key Programmatic Steps

The individual steps in the program, leading to cGMP production of an FMD vaccine candidate include:

1. Process Development
 - a. Establish M2A cells in stirred tank bioreactor at 20 L scale (2 x 10 L bioreactors) using GenVec's advanced, scalable production process
 - b. Optimize parameters for medium exchange, Zn-induction, infection and harvest
 - c. Confirm that current downstream processes are appropriately scaled and optimized to enable efficient yield of vector with acceptable levels of purity and potency
2. Demonstration of Process Reproducibility

- a. Generation of comprehensive set of batch production records and SOPs. GenVec will modify existing documents to incorporate any modifications that pertain to production of FMD vector in M2A cells (See Attachment 2 for current PD documentation).
 - b. Perform 3 successive Reproducibility Runs within GenVec Process Development laboratories
 - c. Perform extensive QC testing for both in-process and final bulk drug samples to demonstrate potency, purity, identity and quality
 - d. Establish acceptance criteria for the unit operation steps in the manufacturing process and QC assays for eventual release of GMP materials produced at CMO
3. Technology Transfer to CMO
 - a. Prepare Technology Transfer Protocol
 - b. Incorporate any FMD-specific process changes into current GMP production documentation (Batch Records, SOPs, raw material specifications)
 - c. Perform product change-over procedure to assure appropriate clearance of other vector components, documentation and materials from the manufacturing suites.
 - d. Establish full complement of QA-released raw materials for cGMP manufacture of FMD vector
4. GMP Production of Clinical Bulk Drug Lot
 - a. Use commercially reasonable efforts to produce one FMD bulk drug lot at 20 L scale using GenVec's advanced scalable manufacturing process
 - b. GenVec will provide technical and QA oversight and review of CMO activities, as needed during production
 - c. GenVec QA will review all production documentation, including Batch Records, Raw Material testing and release documentation, environmental monitoring records, equipment monitoring records and process deviation requests.
5. QC Testing of Bulk Drug Lot and QA Release of Lot
 - a. Comprehensive in-process and bulk drug testing for purity, potency, safety, identity and quality according to GenVec Sampling Plan
 - b. Technical and QA review of all testing documents
 - c. QA release of bulk drug lot
6. Vialing of Vaccine Final Drug Product Lot at CMO (Molecular Medicine)

- a. Qualification of filling operation (3 successive medium fill qualification runs in vialing process)
- b. Formulation and filling of an appropriate number of Vaccine Final Drug Product vials to enable QC release testing, supply 1000 vials to DHS and support of future stability studies. Note: a stability study was not proposed under this current statement of work.
- c. GenVec will provide technical and QA oversight and review of CMO activities, as needed during vialing operations
- d. GenVec QA will review all production documentation, including Batch Records, Raw Material testing and release documentation, environmental monitoring records, equipment monitoring records and process deviation requests.

7. **QC Testing of Vaccine Final Drug Product Lot and QA Release of Lot**

- a. Test of final drug product vials for purity, potency, safety, identity and quality according to GenVec release specification
- b. Technical and QA review of all production and testing documents
- c. QA release of FMD vaccine final drug product lot

Description of Scalable Manufacturing Process

GenVec has successfully developed a scalable Adenovector manufacturing process that GenVec believes is suitable for use as the initial production process for all GenVec-supplied AdFMD vaccine Clinical Trial Materials. The details for the process can be found in i) process flow diagram, ii) process description, iii) key manufacturing equipment, and iv) list of raw materials used in manufacturing process documents that will be made available to DHS upon request.

Description of GenVec QC Testing Program

The details of the GenVec QC Testing Program can be found in i) list and description of QC assays and ii) description of stability program documents that will be made available to DHS upon request.

Description of GenVec QA Program

The details of the GenVec QA Program can be found in i) QA Program (training, auditing, document review, change control, CAPA program, lot release etc), ii) Quality System, iii) release specification and iv) certificate of analysis for final drug product documents that will be made available to DHS upon request.

Conduct 10L bioreactor upstream and downstream optimization studies in advance of full development process development work for technology transfer to

manufacturing. Provide material to DHS for animal safety and efficacy testing (New Funding Activity Option Year 1).

In advance of the key programmatic steps outlined above, which normally occur following master cell and master virus banking, GenVec will continue pre-product development efforts started in March 2007. To do this GenVec will involve a team of scientists with expertise in process development and manufacturing technology transfer. Scientists with expertise in process development will evaluate and explore upstream and downstream methods to optimize the production of the lead Adenovector FMD vaccine candidate. It is expected that pre-product development findings would be incorporated into the later product development of the project at some future time before large-scale production for stockpiling or commercialization.

**SOW ATTACHMENT II – LIST OF TECHNICAL AND PHYSICAL
DELIVERABLES
(OPTION YEAR ONE)**

Milestone	Option year 1 Deliverables	Timeline
Use commercially reasonable efforts to complete construction and testing of additional Ad5-FMD Serotype Vaccine Vectors Using Different Promoters, FMD Capsid and FMD Protease Genes	Complete construction and testing (table 2) of vaccine vaccine vector H	April 30, 2008
	Complete construction and testing (table 2) of vaccine vector I	July 31, 2008
	Complete construction and testing (table 2) of vaccine vector J	October 31, 2008
	Complete construction and testing (table 2) of vaccine vector K	January 31, 2009
	DHS receipt of research reports for each vaccine (H-K)	January 31, 2009 (Report for vaccine vector L February 28, 2009)
	Provide at least four (4) process development lots of lead Ad5-FMD Serotype-Specific candidate to DHS for animal testing (seroconversion and/or challenge studies)	October 30, 2007 January 31, 2008 April 30, 2008 July 31, 2008
	Produce and characterize antibody reagents to support in vitro assay development	Jan 31, 2009
	Complete in vitro potency assay development/pre-validation studies	January 31, 2009
	Complete analytical and biochemical studies focused on vaccine potency improvements	January 31, 2009
Use commercially reasonable efforts for completion, submission and USDA CVB Approval/Guidance of Ad5-FMD Serotype-Specific Category III SIF and SIF for Environmental		
	Provide necessary regulatory activities through duration of contract	Jan 31, 2009
	Provide DHS with a copy of each document submitted to USDA CVB for the previous Quarter	Apr 30, 2008 Jul 31, 2008 Oct 31, 2008 Jan 31, 2009

Release	Complete additional MCB characterization and aging study testing (table 3) and send report to DHS	March 31, 2009
Use commercially reasonable efforts for production, Testing and USDA CVB Approval/Guidance of Ad5-Serotype-Specific Master Virus Bank (MVB) and Working Virus Bank (WVB)	Manufacture of FMD MVB	January 30, 2009
	Testing (table 7) of FMD MVB	March 30, 2009
	Production of FMD MVB	Remaining deliverables to be determined under Option Year 2
	Testing (table 8) of FMD WVB	
	Submit MVB and WVB report to DHS and to USDA CVB and obtain submission approval from CVB	
Use commercially reasonable efforts for production of Clinical Lot for Animal Studies	Assay development	January 30, 2009
	Process development	July 30, 2008
	Process optimization, characterization and technology transfer	May 31, 2009
	Produce clinical lot bulk drug for animal studies (1000 doses)	To be determined under Option Year 2
	Perform testing of clinical lot bulk drug	
	Vialing of clinical lot	
	Complete testing of clinical lot vaccine product	
USDA CVB Approval/Guidance of Clinical Protocols for Pivotal Cattle Studies	Meeting (s) with CVB and DHS to discuss protocols	To be determined under Option Year 2
	Draft clinical protocols (# and type TBD)	
	Submit clinical protocols and obtain approval	
Preparation and satisfactory production of three consecutive prelicensing serials of experimental Ad5-FMD serotype specific product	Produce and satisfactory pass prelicensing serial #1	To be determined under Option Year 2
	Produce and satisfactory pass prelicensing serial #2	
	Produce and satisfactory pass prelicensing serial #3	
Preparation, submission and approval of an Ad5-FMD serotype-specific product application for U.S. Veterinary Biological License	Prepare product application	To be determined under Option Year 2
	Submit product application	
	Obtain final approval of product application	

ARTICLE IV: PAYABLE EVENT SCHEDULE AND DELIVERABLES is amended to add the following:

B. Schedule of Payments and Payable Milestones (Phase IIIa):

Milestone	Option 1 Amount	Milestone Date
1	\$2,005,594	30 Days After Option 1 Start
2	\$622,410	60 Days After Option 1 Start
3	\$677,894	90 Days After Option 1 Start
4	\$0	
5	\$0	
6	\$697,090	120 Days After Option 1 Start
7	\$1,610,827	90 Days After Option 1 Start

All other ARTICLES in the agreement remain unchanged and remain in effect during this Option 1 effort.