AGREEMENT # 75A501-20-C-00114 FLOWDOWN REQUIREMENTS FOR SUBCONTRACTS

(BARDA AZD1222)

(Appendix A)

In Appendix A, "Subcontractor" means the "Supplier" and "Subcontract" means this "Agreement."

Subcontractor understands and acknowledges that AstraZeneca is performing an Other Transaction Agreement ("OTA") with the U.S. Department of Health and Human Services ("HHS"), Biomedical Advanced Research And Development Authority (BARDA), Advance Agreement # (75A501-20-C-00114), in response to Broad Agency Announcement for the Advanced Research and Development of Chemical, Biological, Radiological, and Nuclear Medical Countermeasures": Area of Interest #8.3, ChAdOx1: Manufacturing and Clinical Evaluation of a COVID-19 Vaccine.

As a participant in the OTA, AstraZeneca must comply with specific provisions of the OTA, including ensuring that any subcontractors supporting AstraZeneca comply with the terms in the OTA that flow down to subcontractors. These requirements will be outlined in the final AZ OTA (Other Transactional Agreement), upon its execution. To the extent applicable to the Subcontractor's activities under this Agreement, the Subcontrractor agrees to comply with relevant US Government terms and conditions, as notified to it by AstraZeneca in writing upon execution of AZ final OTA, including Terms and Conditions/Flowdowns listed in this Appendix. Should any of the terms and conditions contained in Appendix A contradict those elsewhere in the Agreement, or any SoW under the Agreement, then the terms and conditions of Appendix A shall supersede all others.

Subcontractor acknowledges and understands that the Government is a third-party beneficiary to this Agreement and is entitled to the rights and benefits hereunder and may enforce the provisions hereof as if it were a party hereto.

Communication/notification required under this Agreement from/to the Subcontractor to/from BARDA shall be made through AstraZeneca.

1. DEFINITIONS

AstraZeneca Information:

A. Any information of AstraZeneca or its Affiliates provided before, on or after the Effective Date by or on behalf of AstraZeneca or its Affiliates to Subcontractor or its Affiliates either in connection with the discussions and negotiations pertaining to, or in the course of performing, this Agreement, whether of a technical, business or other nature, including information that relates to AstraZeneca's or any of its Affiliates' trade secrets, products, promotional material, developments, proprietary rights or business affairs, the Protocol or any Inventions,

B. Any and all data, information, Background IPR or material that is provided or communicated by or on behalf of AstraZeneca or its Affiliates, or otherwise becomes known, to Supplier, or is collected or generated by or on behalf of Supplier, in connection with this Agreement or the activities contemplated hereunder, including, without limitation, information relating to AstraZeneca's or its Affiliates' business and products (including Products) and all Results (as defined below) and Personal Data (which - if applicable - is defined in the Statement of Work).

Computer Software:

A. Computer programs that comprise a series of instructions, rules, routines, or statements, regardless of the media in which recorded, that allow or cause a computer to perform a specific operation or series of operations; and

B. Recorded information comprising source code listings, design details, algorithms, processes, flow charts, formulas, and related material that would enable the computer program to be produced, created, or compiled.

C. Does not include computer databases or computer software documentation.

Data: Recorded information, regardless of form or method of recording, which includes but is not limited to, technical data, software, and trade secrets made in the performance of work under this Agreement within the Field. The term does not include financial, administrative, cost, pricing or management information, and specifically excludes AstraZeneca Information.

Field: The development of antibacterial assets to treat hospital and biothreat infections.

Foreign Firm or Institution: A firm or institution organized or existing under the laws of a country other than the United States, its territories, or possessions. The term includes, for purposes of this Agreement, any agency or instrumentality of a foreign government; and firms, institutions or business organizations which are owned or substantially controlled by foreign governments, firms, institutions, or individuals.

Government: The United States of America, as represented by HHS.

Government Purpose Rights: The rights to use, duplicate, or disclose Data and Results, in whole or in part and in any manner, for Government purposes only, and to have or permit others to do so for Government purposes only.

Invention: Any inventions, discoveries, know-how and other intellectual property, including any improvements thereto, that are conceived, reduced to practice or otherwise made by Supplier, its Affiliates, or its or their respective employees or representatives (whether solely or jointly with others) in the performance of their obligations under this Agreement, and any patent, trade secret or other intellectual property rights with respect thereto.

Know-How: Information, practical knowledge, techniques, and skill development by Subcontractor in the performance of work under this Agreement necessary for the Practical Application of an Invention within the Field.

Limited Rights: The rights to use, modify, reproduce, perform, display, or disclose Data and Results, in whole or in part, within the Government solely for research purposes for the Field. The Government will ensure that disclosed information is safeguarded in accordance with the restrictions of this Agreement. The Government may not, without the prior written permission of AstraZeneca, release or disclose the Data or Results outside the Government, use the Data or Results for competitive procurement or manufacture, release or disclose the data for commercial purposes, or authorize the Data or Results except as permitted by this Agreement.

Practical Application: With respect to a Subject Invention, to manufacture, in the case of a composition of product; to practice, in the case of a process or method, or to operate, in the case of a machine or system; and, in each case, under such conditions as to establish that the Subject Invention is capable of being utilized and that its benefits are, to the extent permitted by law or Government regulations, available to the public.

Program: Research and development being conducted by the Parties pursuant to this Agreement.

Property: Any tangible personal property other than property actually consumed during the execution of work under this Agreement.

Results: Any ideas, inventions, discoveries, data, documentation, reports, materials, samples, products, writings, designs, computer software, processes, principles, methods, techniques and other information, recorded in any form, that are discovered, conceived, created, reduced to practice or otherwise generated as a result of or in connection with the Services by or on behalf of Supplier (whether solely or jointly with others), and any patent, trade secret, copyright or other intellectual property rights pertaining to any of the foregoing.

Subject Invention: Any Invention conceived in the performance of work under this Agreement within the Field for which Subcontractor pursues a patent.

Technology: Discoveries, innovations, Know-How and Subject Inventions, whether patentable or not, conceived in the performance of work under this Agreement, including computer software, recognized under U.S. law as intellectual creations to which rights of ownership accrue, including, but not limited to, patents, trade secrets, and copyrights developed under this Agreement.

Under this Agreement: When used, for example but without limitation, in the definitions of Data, Know-How, Property, Subject Inventions and Technology, means activities conducted pursuant to this Agreement that are Government funded or cost shared with the Government.

2. KICK-OFF AND QUARTERLY MEETINGS

Subcontractor may need to participate in project meetings with Government and AstraZeneca. These meetings may include face-to-face meetings with BARDA/AMCG in Washington, D.C or other US Government locations, and at work sites of the Subcontractor. Such meetings may include, but are not limited to, meetings with the Subcontractor to discuss study designs, site visits to the Subcontractor's facilities, and meetings with AstraZeneca and Government officials to discuss the technical, financial, regulatory and ethical aspects of the program.

3. CONFIDENTIAL INFORMATION

Subcontractor understands and agrees that AstraZeneca may provide Confidential Information provided in this Agreement (including information exchanged pursuant to an existing confidentiality or nondisclosure agreement) to representatives or agents of the Government in connection with AstraZeneca's performance under the OTA. AstraZeneca will take commercially reasonable steps to restrict their disclosure by the Government under applicable public disclosure/transparency laws. AstraZeneca, however, shall have no liability for the Government's release of any Supplier Confidential Information.

4. TERMINATION FOR CONVENIENCE

Unless the termination clauses are negotiated in MSA or any other agreements, AstraZeneca may terminate the Agreement for convenience by providing at least 60 days prior written notice to the Subcontractor. In the event of a termination of the Agreement, it is agreed that disposition of Data developed under this Agreement shall be in accordance with the provisions set forth in Section 7, Data Rights. In the event of termination by AstraZeneca under this Section 4, the Subcontractor's termination costs shall be determined pursuant to the terms of Federal Acquisition Regulation ("FAR") 31.205-42. AstraZeneca and the Subcontractor will negotiate in good faith a reasonable and timely adjustment of all outstanding issues between the Parties as a result of termination. Failure of the Parties to agree to a reasonable adjustment will be resolved pursuant to Section 6, Disputes. In the event of termination, neither party shall have any continuing obligations to perform under the Program except as otherwise specified herein.

5. MODIFICATIONS

At the Government's request, AstraZeneca may at any time, by written order, make changes within the general scope of this Agreement in any one or more of the following: (a) drawings, designs, or specifications when the supplies to be furnished are to be specially manufactured for the Government in accordance with the drawings, designs, or specifications; (b) method of shipment or packing; (c) place of delivery. If any such change causes an increase or decrease in the cost of, or the time required for, performance of any part of the work under this Agreement, whether or not changed by the order, AstraZeneca shall make an equitable adjustment in the Agreement price, the delivery schedule, or both, and shall modify the Agreement. Subcontractor must assert its right to an adjustment under this clause within 20 days from the date of receipt of the written order. If the Subcontractor's proposal includes the cost of property made obsolete or excess by the change, AstraZeneca shall have the right to prescribe the manner of the disposition of the property. Failure to agree to any adjustment shall be a dispute under Section 6, Disputes. However, nothing in this clause shall excuse the Subcontractor from proceeding with the Agreement as changed.

6. DISPUTES

The parties shall attempt to resolve any dispute arising under this Agreement through good faith discussions between each Party. If the Parties are unable to resolve any dispute, either Party may bring an appropriate civil suit in any court of competent jurisdiction in Delaware. Delaware law shall apply to the interpretation of this Agreement. Subcontractor shall continue to diligently perform the Agreement during the pendency of any dispute.

7. DATA RIGHTS

As between AstraZeneca and Subcontractor, ownership and rights to Data are set forth elsewhere in the Agreement. To the extent that Subcontractor retains rights to Data, these rights are subservient to the following Government rights and subject to the following Government conditions:

A. Allocation of Principal Rights

i. For Data other than computer software, the Subcontractor grants to the Government a paid-up, nonexclusive, nontransferable, nonsublicensable, irrevocable, worldwide license in such Data to reproduce, prepare derivative works, distribute copies to the public, and perform publicly and display publicly by or on behalf of the Government, subject to the limitations applicable to the Government's use of Limited Rights Data and except as expressly provided elsewhere in this Agreement. For computer software, the Subcontractor grants to the Government, and others acting on its behalf, a paid-up, nonexclusive, irrevocable, worldwide license in such copyrighted computer software to reproduce, prepare derivative works, and perform publicly and display publicly (but not to distribute copies to the public) by or on behalf of the Government.

ii. Data in any document that would disclose a Subject Invention will be subject to Limited Rights until publication of patent application in accordance with Section 8, Patent Rights, of this Agreement.

iii. Subcontractor agrees to retain and maintain in good condition all Data necessary to achieve Practical Application of any Subject Invention in accordance with the Subcontractor's established record retention practices. In the event of exercise of the Government's March-in Rights as set forth under Section 8, Subcontractor agrees, upon written request from the Government, to deliver at no additional cost to the Government, all existing Data necessary to achieve Practical Application of the relevant Subject Invention within 60 calendar days from the date of the written request. The Government shall retain Limited Rights to this delivered Data.

B. Marking of Data. Subcontractor will mark any Data delivered under this Agreement with Limited Rights with the following legend:

> "LIMITED RIGHTS" The right to use, modify, reproduce, perform, display, or disclose this Data is restricted by Agreement HHSO100201500029C between the Government and the AstraZeneca (disclosure is limited within the Government). Any reproduction of this Data or portions thereof marked with this legend must also reproduce the markings."

C. Lower Tier Agreements. Subcontractor shall include this Section 7, Data Rights, suitably modified to identify the Parties, in all lower tier agreements for experimental, developmental, or research work.

D. Identification and Disposition of Data. The Subcontractor shall keep copies of all Data required by the Food and Drug Administration (FDA) relevant to this Agreement for the time specified by the FDA. In addition, the Subcontractor shall provide regulatory data to AstraZeneca in accordance to pre-determined Reporting Requirements. AstraZeneca and the Government reserve the right to review any other data determined by AstraZeneca or HHS to be relevant to this Agreement

E. Publication and Publicity**.** No Data obtained under this Agreement shall be released or publicized without concurrence from AstraZeneca. For purposes of this Agreement, "Publication" is defined as an issue of printed material offered for distribution or any communication or oral presentation of information,

including any manuscript or scientific meeting abstract. Any Publication containing Data generated under this Agreement must be submitted to AstraZeneca for review and comment no less than 45 calendar days for manuscripts and 25 calendar days for abstracts before submission for public presentation or publication. Government support shall be acknowledged in all such publications substantially as follows:

> "This project has been funded in whole or in part with Federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority, under OT number HHSO100201500029C.

F. Review of Press Releases. Subcontractor shall not make any press releases regarding this Agreement without permission from AstraZeneca. Subcontractor agrees to accurately and factually represent the work conducted under this Agreement in all press releases. Misrepresenting results or releasing information that is injurious to the integrity of the Government and AstraZeneca and may be construed as improper conduct. Press releases shall be considered to include the public release of information to any medium, excluding peer-reviewed scientific publications. Subcontractor agrees to provide AstraZeneca with an advance copy of any press release related to this Agreement not less than 20 business days prior to the issuance of the press release. Government support shall be acknowledged in all such press releases substantially as follows:

> "This project has been funded in whole or in part with Federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority, under OT number HHSO100201500029C.

8. PATENT RIGHTS

As between AstraZeneca and Subcontractor, ownership and rights to Inventions are set forth elsewhere in the Agreement. To the extent that Subcontractor retains any rights to Subject Inventions, these rights are subservient to the following Government rights and subject to the following Government conditions:

A. Allocation of Principal Rights. Unless Subcontractor shall have notified AstraZeneca (in accordance with Section 8(B) below) that Subcontractor does not intend to retain title, in which case title shall vest with the Government, Subcontractor shall retain the right, title, and interest throughout the world to each Subject Invention, consistent with the provisions of this Paragraph and 35 U.S. § 202. With respect to any Subject Invention in which Subcontractor retains title, the Government shall have a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced on its behalf the Subject Invention throughout the world.

B. Invention Disclosure, Election of Title, and Filing of Patent Application

i. Subcontractor shall disclose each Subject Invention to AstraZeneca within four months after the inventor discloses it in writing to his/her company personnel responsible for patent matters. The disclosure to AstraZeneca shall be in the form of a written report and shall identify the the identity of the inventor(s). It shall be sufficiently complete in technical detail to convey a clear understanding to the extent known at the time of the disclosure, of the nature, purpose, operation, and the physical, chemical, biological, or electrical characteristics of the Subject Invention. The disclosure shall also identify any publication, sale, or public use of the Subject Invention and whether a manuscript describing the Subject Invention has been submitted for publication and, if so, whether it has been accepted for publication at the time of disclosure.

ii. If Subcontractor determines that it does not intend to retain title to any such Subject Invention, Subcontractor shall notify AstraZeneca, in writing, within two years of disclosure to AstraZeneca. However, in any case where publication, sale, or public use has initiated the one-year statutory period wherein valid patent protection can still be obtained in the United States, the period for such notice may be shortened by AstraZeneca or the Government to a date that is no more than 60 calendar days prior to the end of the statutory period.

iii. Subcontractor shall file its initial patent application on a Subject Invention to which it elects to retain title within one year after election of title or, if earlier, prior to the end of the statutory period wherein valid patent protection can be obtained in the United States after a publication, or sale, or public use. Subcontractor may elect to file patent applications in additional countries (including the European Patent Office and the Patent Cooperation Treaty) within either ten months of the corresponding initial patent application or six months from the date permission is granted by the Commissioner of Patents and Trademarks to file foreign patent applications, where such filing has been prohibited by a Secrecy Order.

iv. Requests for extension of the time for disclosure election, and filing under Section 8(B) may, at the discretion of the Government, and after considering the position of Subcontractor, be granted.

C. Conditions When the Government May Obtain Title. Upon the Government's written request, Subcontractor shall convey title to any Subject Invention to the Government under any of the following conditions:

i. If Subcontractor fails to disclose or elects not to retain title to the Subject Invention within the times specified in Section 8(B); provided, that the Government may only request title within 60 calendar days after learning of the failure of Subcontractor to disclose or elect within the specified times;

ii. In those countries in which Subcontractor fails to file patent applications within the times specified in Section 8(B); provided, that if Subcontractor has filed a patent application in a country after the times specified in Section 8(B) of this Article, but prior to its receipt of the written request by the Government, Subcontractor shall continue to retain title in that country; or

iii. In any country in which Subcontractor decides not to continue the prosecution of any application for, to pay the maintenance fees on, or defend in reexamination or opposition proceedings on, a patent on a Subject Invention.

D. Minimum Rights to Subcontractor and Protection of Subcontractor's Right to File

i. Subcontractor shall retain a nonexclusive, royalty-free license throughout the world in each Subject Invention to which the Government obtains title, except if Subcontractor fails to disclose the invention within the times specified in Section 8(B). Subcontractor's license extends to the Subcontractor's subsidiaries and affiliates, if any, within the corporate structure of which Subcontractor is a party and includes the right to grant licenses of the same scope to the extent that Subcontractor was legally obligated or permitted to do so at the time the Agreement was executed. The license is otherwise transferable only with the approval of the Government, except when transferred to the successor of that part of Subcontractor's business to which the Subject invention pertains. Government approval for license transfer shall not be unreasonably withheld.

ii. The Subcontractor license may be revoked or modified by the Government to the extent necessary to achieve expeditious Practical Application of the Subject Invention pursuant to an application for an exclusive or nonexclusive license submitted consistent with appropriate provisions at 37 CFR Part 404. Subcontractor's license shall not be revoked in that field of use or the geographical areas in which Subcontractor has achieved Practical Application of the Subject Invention and continues to make the benefits of the Subject Invention accessible to the public.

iii. Before revocation or modification of Subcontractor's license, the Government shall furnish Subcontractor a written notice of its intention to revoke or modify the license, and Subcontractor shall be allowed 30 calendar days (or such other time as may be authorized for good cause shown) after the notice to show cause why the license should not be revoked or modified.

E. Action to Protect the Government's Interest

i. Subcontractor agrees to execute or to have executed and promptly deliver to the Government all instruments necessary to (a) establish or confirm the rights the Government has throughout the

world in those Subject Inventions to which Subcontractor elects to retain title, and (b) convey title to the Government when requested under Section 8(C) and to enable the Government to obtain patent protection throughout the world in that Subject Invention.

ii. Subcontractor agrees to require, by written agreement, its employees, other than clerical and non-technical employees, to disclose promptly in writing to personnel identified as responsible for the administration of patent matters and in a format suggested by Subcontractor each Subject Invention made under this Agreement in order that Subcontractor can comply with the disclosure provisions of Section 8(B). Subcontractor shall instruct employees, through employee agreements or other suitable educational programs, on the importance of reporting inventions in sufficient time to permit the filing of patent applications prior to U.S. or foreign statutory bars.

iii. Subcontractor shall notify the Government of any decisions not to continue the prosecution of a patent application for a Subject Invention, pay maintenance fees, or defend in a reexamination or opposition proceedings on a patent of a Subject Invention, in any country, not less than 30 calendar days before the expiration of the response period required by the relevant patent office.

iv. Subcontractor shall include, within the specification of any U.S. patent application and any patent issuing thereon covering a Subject Invention, the following statement: "This invention was made with Government support under Agreement HHSO100201500029C, awarded by HHS. The Government has certain rights in the invention."

F. Lower Tier Agreements. Subcontractor shall include this Paragraph, including this subparagraph (f) suitably modified, to identify the Parties, in all lower tier agreements for experimental, developmental, or research work.

G. Reporting on Utilization of Subject Inventions. Subcontractor agrees to submit, during the term of the Agreement, an annual report on the utilization of a Subject Invention or on efforts at obtaining such utilization that is being made by Subcontractor or its licensees or assignees. Such reports shall include information regarding the status of development, date of first commercial sale or use, gross royalties received by Subcontractor, and such other data and information as the **Government** may reasonably specify. Subcontractor also agrees to provide additional reports as may be requested by **the Government** in connection with any march-in proceedings undertaken by **the Government** in accordance with **Section 8(H)**.

H. March-in Rights**.** The Subcontractor agrees that, with respect to any Subject Invention in which it has retained title, **the Government** has the right to require Subcontractor, an assignee, or exclusive licensee of a Subject Invention to grant a non-exclusive license within the Field to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if Subcontractor, assignee, or exclusive licensee refuses such a request, **the Government** has the right to grant such a license within the Field itself if **the Government** determines that:

i. Such action is necessary because Subcontractor or assignee has not taken effective steps, consistent with the intent of this Agreement, to achieve Practical Application of the Subject Invention; or

ii. Such action is necessary to alleviate health or safety needs which are not reasonably satisfied by Subcontractor, assignee, or their licensees.

9. AUDIT RIGHTS

Subcontractor shall maintain adequate records to account for all costs incurred under this Agreement for which Subcontractor seeks reimbursement. Subcontractor's relevant financial records are subject to examination or audit on behalf of AstraZeneca and the Government for a period not to exceed three years after expiration of the term of this Agreement. AstraZeneca shall have direct access to sufficient records and information of the Subcontractor to ensure full accountability for all amounts reimbursed under this Agreement. Such audit, examination, or access shall be

performed during business hours on business days upon at least two weeks prior written notice and shall be subject to the security requirements of the audited party.

AstraZeneca has rights to conduct quality assurance audits and site visits of Subcontractor. The US Governmentreserves the right to participate in the audits and/or any necessary site visits through AstraZeneca.

10. PROHIBITION ON CONTRACTOR INVOLVEMENT WITH TERRORIST ACTIVITIES

Subcontractor acknowledges that U.S. Executive Orders and Laws, including but not limited to E.O. 13224 and P.L. 107-56, prohibit transactions with, and the provision of resources and support to, individuals and organizations associated with terrorism. It is the legal responsibility of the Subcontractor to ensure compliance with these Executive Orders and Laws. This clause must be included in all lower tier agreements issued under this Agreement.

11. COMPTROLLER GENERAL ACCESS TO RECORDS

To the extent that the total Government payment under this Subcontract exceeds $5,000,000, the Comptroller General, at its discretion, shall have access to and the right to examine records relating to performance under this Agreement of any entity that participates in the performance of this Agreement for a period of three years after final payment is made. This paragraph only applies to any record that is created or maintained in the ordinary course of business or pursuant to a provision of law. The terms of this paragraph shall be included in all lower tier sub-agreements to the Agreement.

12. CIVIL RIGHTS ACT

Performance of this Agreement in the US is subject to the compliance requirements of Title VI of the Civil Rights Act of 1964 as amended (42 U.S.C. 2000-d) relating to nondiscrimination in Federally assisted programs.

13. FOREIGN ACCESS TO TECHNOLOGY

This Article shall remain in effect during the term of the Agreement and for five years thereafter.

A. General

i. The Parties agree that research findings and technology developments arising under this Agreement may constitute a significant enhancement to the national security, and to the economic vitality of the United States. Accordingly, access to important technology developments under this Agreement by Foreign Firms or Institutions must be carefully controlled. Subcontractor agrees to comply with all applicable laws regarding export controls and not to export any Technology to any US embargoed countries.

ii. The Subcontractor shall provide timely notice to AstraZeneca of any proposed transfers from the Subcontractor of Technology developed under this Agreement to Foreign Firms or Institutions; provided that, this Article shall not apply to transfers by Subcontractor of Technology to affiliates of Subcontractor or as part of the sale, merger, or acquisition of Subcontractor, or as part of the sale or transfer of that part of Subcontractor's business to which the Technology developed under this Agreement pertains. If the Government determines that a transfer may have adverse consequences to the national security interests of the United States, the Subcontractor, its vendors, AstraZeneca and the Government shall jointly endeavor to find alternatives to the proposed transfer which obviate or mitigate potential adverse consequences of the transfer but which provide substantially equivalent benefits to the Subcontractor.

iii. In any event, the Subcontractor shall provide written notice to the AstraZeneca of any proposed transfer to a foreign firm or institution at least 30 calendar days prior to the proposed date of transfer. Such notice shall cite this Article and shall state specifically what is to be transferred and the general terms of the transfer. No transfer shall take place until a decision is rendered by AstraZeneca.

iv. In the event of a transfer of Technology by Subcontractor to a Foreign Firm or Institution which is identified as a Prohibited Source pursuant to Federal Acquisition Regulation Subpart 25.7:

a. AstraZeneca may terminate this Agreement for cause and

b. the Government shall have a non-exclusive, nontransferable, irrevocable, paid-up license to practice or have practiced on behalf of the United States the Technology throughout the world for Government and any and all other purposes, particularly to effectuate the intent of this Agreement. Upon request of AstraZeneca, the Subcontractor shall provide written confirmation of such licenses.

B. Lower Tier Agreements. Subcontractor shall include Section 14, suitably modified, to identify the Parties, in all lower tier agreements for experimental, developmental, or research work.

14. PROTECTION OF HUMAN SUBJECTS

Subcontractor agrees that the rights and welfare of human subjects involved in any research under this Agreement shall be protected in accordance with 45 CFR Part 46 and with the Subcontractor's current Assurance of Compliance on file with the Office for Human Research Protections (OHRP), Office of Public Health and Science (OPHS). Subcontractor further agrees to provide certification that the Institutional Review Board has reviewed and approved the procedures, which involve human subjects, in accordance with 45 CFR Part 46 and the Assurance of Compliance.

Subcontractor shall bear full responsibility for the performance of all work and services involving the use of human subjects under this Agreement and shall ensure that work is conducted in a proper manner and as safely as is feasible. The Parties hereto agree that Subcontractor retains the right to control and direct the performance of all work under this Agreement. Nothing in this Agreement shall be deemed to constitute Subcontractor or any sub consortium, agent or employee of Subcontractor, or any other person, organization, institution, or group of any kind whatsoever, as the agent or employee of AstraZeneca or the Government. Subcontractor agrees that it has entered into this Agreement and will discharge its obligations, duties, and undertakings and the work pursuant thereto, whether requiring professional judgment or otherwise, as an independent consortium without imputing liability on the part of AstraZeneca or the Government for the acts of the Subcontractor or its employees.

If at any time during the performance of this Agreement, AstraZeneca determines, in consultation with the OHRP, OPHS, ASH, that the Subcontractor is not in compliance with any of the requirements and/or standards stated in the paragraphs above, AstraZeneca may immediately suspend, in whole or in part, work and further payments under this Agreement until the Subcontractor corrects the noncompliance. Notice of the suspension may be communicated by telephone and confirmed in writing. If the Subcontractor fails to complete corrective action within the period of time designated in AstraZeneca's written notice of suspension, AstraZeneca may terminate this Agreement in whole or in part.

A. HUMAN MATERIALS

The acquisition and supply of all human specimen material (including fetal material) used under this Agreement shall be obtained by Subcontractor in full compliance with applicable Federal, State and Local laws and no undue inducements, monetary or otherwise, will be offered to any person to influence their donation of human material.

The Subcontractor shall provide written documentation that all human materials obtained as a result of research involving human subjects conducted under this Agreement, by collaborating sites, or by lower tier Subcontractors identified under this Agreement, were obtained with prior approval by the Office for Human Research Protections (OHRP) of an Assurance to comply with the requirements of 45 CFR 46 to protect human research subjects. This restriction applies to all collaborating sites without OHRP-approved Assurances, whether domestic or foreign, and compliance must be ensured by the Subcontractor.

Provision by the Subcontractor to AstraZeneca of a properly completed "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263 (formerly Optional Form 310), certifying IRB review and approval of the protocol from which the human materials were obtained constitutes the written documentation required. The human subject certification can be met by submission of a self-designated

form provided that it contains the information required by the "Protection of Human Subjects Assurance Identification/IRB Certification/ Declaration of Exemption", Form OMB No. 0990-0263(formerly Optional Form 310).

B. RESEARCH INVOLVING HUMAN FETAL TISSUE

All research involving human fetal tissue shall be conducted in accordance with the Public Health Service Act, 42 U.S.C. 289g-1 and 289g-2. Implementing regulations and guidance for conducting research on human fetal tissue may be found at 45 CFR 46, Subpart B. Subcontractor shall make available, for audit by AstraZeneca, the physician statements and informed consents required by 42 USC 289g-1(b) and (c), or ensure AstraZeneca access to those records, if maintained by an entity other than the Subcontractor.

C. CARE OF LIVE VERTEBRATE ANIMALS

Before undertaking performance of this Agreement involving animal related activities, the Subcontractor shall register with the Secretary of Agriculture of the United States in accordance with 7 U.S.C. 2136 and 9 CFR 2.25 through 2.28. Subcontractor shall furnish evidence of the registration to AstraZeneca.

Subcontractor shall acquire vertebrate animals used in research from a dealer licensed by the Secretary of Agriculture under 7 U.S.C. 2133 and 9 CFR 2.1 through 2.11, or from a source that is exempt from licensing under those sections.

Subcontractor agrees that the care and use of any live vertebrate animals used or intended for use in the performance of this Agreement will conform with the PHS Policy on Humane Care of Use of Laboratory Animals, the current Animal Welfare Assurance, the Guide for the Care and Use of Laboratory Animals prepared by the Institute of Laboratory Animal Resources and the pertinent laws and regulations of the United States Department of Agriculture (see 7 U.S.C. 2131 et seq. and 9 CFR Subchapter A, Parts 1 - 4). In case of conflict between standards, the more stringent standard shall be used.

If at any time during performance of this Agreement, AstraZeneca determines Subcontractor is not in compliance with any of the requirements and/or standards stated in paragraphs (1) through (3) above, AstraZeneca may immediately suspend, in whole or in part, work and further payments under this Agreement until the Subcontractor corrects the noncompliance. Notice of the suspension may be communicated by telephone and confirmed in writing. If the Subcontractor fails to complete corrective action within the period of time designated in AstraZeneca's written notice of suspension, AstraZeneca may terminate this Agreement in whole or in part.

Note: Subcontractor may request registration of its facility and a current listing of licensed dealers from the Regional Office of the Animal and Plant Health Inspection Service (APHIS), USDA, for the region in which its research facility is located. Information concerning this program may be obtained by contacting your regional office below or the Animal Care Staff, USDA/APHIS, 4700 River Road, Riverdale, Maryland 20737.

D. ANIMAL WELFARE

All research involving live, vertebrate animals shall be conducted in accordance 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. Primate studies will not begin until the CRO's IACUC and the Subcontractor's Animal Welfare Department provide final approval of the study protocol.

E. PROTECTION OF PERSONNEL WHO WORK WITH NONHUMAN PRIMATES

Subcontractor personnel who work with nonhuman primates or enter rooms or areas containing nonhuman primates shall comply with the procedures set forth in NIH Policy Manual 3044-2, entitled, "Protection of NIH Personnel Who Work with Nonhuman Primates," located at the following URL: http://www1.od.nih.gov/oma/manualchapters/intramural/3044-2/.

F. INFORMATION ON COMPLIANCE WITH ANIMAL CARE REQUIREMENTS

Registration with the U.S. Dept. of Agriculture (USDA) is required to use regulated species of animals for biomedical purposes. USDA is responsible for the enforcement of the Animal Welfare Act (7 U.S.C. 2131 et. seq.), http://www.nal.usda.gov/awic/legislat/awa.htm.

The Public Health Service (PHS) Policy is administered by the Office of Laboratory Animal Welfare (OLAW) http://grants2.nih.gov/grants/olaw/olaw.htm. An essential requirement of the PHS Policy http://grants2.nih.gov/grants/olaw/references/phspol.htm is that every institution using live vertebrate animals must obtain an approved assurance from OLAW before they can receive funding from any component of the U.S. Public Health Service. If the Subcontractor does not have an assurance and will be utilizing a lower tier agreement to perform the animal work then Subcontractor must have an Inter-Institutional Assurance in place to allow the Subcontractor to utilize the assurance of the lower tier to meet the HHS requirements for assurance.

The PHS Policy requires that Assured institutions base their programs of animal care and use on the Guide for the Care and Use of Laboratory Animals http://www.nap.edu/readingroom/books/labrats/ and that they comply with the regulations (9 CFR, Subchapter A) http://awic.nal.usda.gov/final-rules-animal-welfare-9-cfr-parts-1-2-and-3 issued by the U.S. Department of Agriculture (USDA) under the Animal Welfare Act. The Guide may differ from USDA regulations in some respects. Compliance with the USDA regulations is an absolute requirement of this Policy.

The Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) http://www.aaalac.org is a professional organization that inspects and evaluates programs of animal care for institutions at their request. Those that meet the high standards are given the accredited status. As of the 2002 revision of the PHS Policy, the only accrediting body recognized by PHS is the AAALAC. While AAALAC accreditation is not required to conduct biomedical research, it is highly desirable. AAALAC uses the Guide as their primary evaluation tool. They also use the Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching. It is published by the Federated of Animal Science Societies http://www.fass.org.

G. APPROVAL OF REQUIRED ASSURANCE BY LAW

Subcontractor shall not conduct research involving live vertebrate animals, nor shall live vertebrate animals be involved in research activities by the Subcontractor under this Agreement unless a satisfactory assurance of compliance with 7 U.S.C. 2136 and 9 CFR Sections 2.25-2.28 is submitted by Subcontractor 30 days prior to commencing research involving live vertebrate animals and approved by the Office of Laboratory Animal Welfare (OLAW). Each performance site (if any) must also assure compliance with 7 U.S.C. 2136 and 9 CFR Sections 2.25-2.28 with the following restriction: Only activities which do not directly involve live vertebrate animals (i.e. are clearly severable and independent from those activities that do involve live vertebrate animals) may be conducted by individual performance sites pending OLAW approval of their respective assurance of compliance with 7 U.S.C. 2136 and 9 CFR Sections 2.25-2.28. Additional information regarding OLAW may be obtained via the Internet at http://grants.nih.gov/grants/olaw/olaw.htm.

Registration with the Select Agent Program for Work Involving the Possession, Use, and/or Transfer of Select Biological Agents or Toxins

Work involving select biological agents or toxins shall not be conducted under this Agreement until the Subcontractor is granted a certificate of registration or are authorized to work with the applicable select agents.

If Subcontractor is a domestic institution who possesses, uses, and/or transfers Select Agents under this Agreement, Subcontractor must complete registration with the Centers for Disease Control and Prevention (CDC), Department of Health and Human Services (DHHS) or the Animal and Plant Health Inspection Services (APHIS), U.S. Department of Agriculture (USDA), as applicable, before performing work involving Select Agents, in accordance with 42 CFR 73. Performance of the Agreement cannot continue if the final registration certificate is denied.

If Subcontractor is a foreign institution who possesses, uses, and/or transfers Select Agents under this Agreement, Subcontractor must provide information satisfactory to AstraZeneca and the Government that a process equivalent to that described in 42 CFR 73 (http://www.cdc.gov/od/sap/docs/42cfr73.pdf) for U.S. institutions is in place and will be administered on behalf of all Select Agent work before performance of the Agreement requiring use of the Select

Agent commences. Subcontractor must provide information addressing the following key elements appropriate for the foreign institution: safety, security, training, procedures for ensuring that only approved/appropriate individuals have access to the Select Agents, and any applicable laws, regulations and policies equivalent to 42 CFR 73. AstraZeneca and the Government will assess the policies and procedures for comparability to the U.S. requirements described in 42 CFR Part 73. When requested by AstraZeneca, the Subcontractor shall provide key information delineating any laws, regulations, policies, and procedures applicable to the foreign institution for the safe and secure possession, use, and transfer of Select Agents. This includes summaries of safety, security, and training plans, and applicable laws, regulations, and policies. For the purpose of security risk assessments, the Subcontractor must provide the names of all individuals at the foreign institution who will have access to the Select Agents and procedures for ensuring that only approved and appropriate individuals have access to Select Agents under the Agreement.

Listings of HHS select agents and toxins, biologic agents and toxins, and overlap agents or toxins as well as information about the registration process, can be obtained on the Select Agent Program Web site at http://www.cdc.gov/od/sap/.

H. MANUFACTURING STANDARDS

The Current Good Manufacturing Practice Regulations (cGMP) (21 CFR 210-211) will be the standard applied for manufacturing, processing and packing of this therapeutic product.

If at any time during the life of this Agreement, the Subcontractor fails to comply with cGMP in the manufacturing, processing and packaging of this therapeutic product and such failure results in a material adverse effect on the safety, purity or potency of this therapeutic product (a material failure) as identified by CDER, the Subcontractor shall have sixty (60) calendar days from the time such material failure is identified to initiate corrective action designed to cure such material failure within three (3) months. If the Subcontractor fails to initiate such an action within the sixty (60) calendar day period, then the Agreement may be terminated for default.

I. MAN-IN-PLANT

With five days advance notice to the Subcontractor in writing from AstraZeneca, the Government or AstraZeneca may place a man-in-plant in the Subcontractor's facility, who shall be subject to the Subcontractor's policies and procedures regarding security and facility access at all times while in the Subcontractor's facility. No Government representative shall publish, divulge, disclose, or make known in any manner, or to any extent not authorized by law, any information coming to him in the course of employment or official duties, while stationed in a Subcontractor plant.