DEPARTMENT OF HEALTH AND HUMAN SERVICES

ADVANCED AGREEMENT BETWEEN THE ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE (ASPR), BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY (BARDA)

AND

ASTRAZENECA

OTHER TRANSACTION AGREEMENT NUMBER: 75A501-20-C-00114

TITLE FOR: ChAdOx1nCoV-19 Vaccine Clinical Development and Manufacturing

DEFINITION: This Advanced Agreement is a written preliminary agreement that authorizes the Recipient to begin work immediately under the limitations and terms specified below in anticipation of the execution of an Other Transaction Agreement.

TERMS:

Other Transaction for Advanced Research (OTAR) means: A legally binding, non-acquisition instrument (generally called "an agreement") used in instances where the principal purpose is the stimulation and/or support of advanced research and development (as defined below), where a non-traditional Government Awardee participates to significant extent in the work.

Other Transaction Agreement Officer (OTAO): Is the responsible government official authorized to bind the government by signing this Agreement and bilateral modifications.

Other Transaction Agreement Specialist (OTAS): Is a supporting official that executes agreement modifications on behalf of the Other Transaction Agreement Officer.

Other Transaction Agreement Technical Representative (OTTR): Is the primary government official for all technical matters on the Agreement.

I. LIMITATION OF GOVERNMENT LIABILITY

(a) In performing the Advanced Agreement, the Recipient is not authorized to make expenditures or incur obligations exceeding $ 413,200,000.00.

(b) The maximum amount for which the Government shall be liable if this agreement is terminated is $ 413,200,000.00.

NOTE: The maximum liability of the Government is the estimated amount necessary to cover the Recipient's requirements for funds before definitization. However, it shall not exceed $413,200,000.00 in the Advanced Agreement unless approved in advance by the OTAO. The Recipient shall have no obligation to commence any of the activities as set

forth in this Advanced Agreement that exceed the obligated amount; however, Recipient must notify the Government in writing if its progress is being impeded by lack of funding.

II. DEFINITIZATION SCHEDULE

(a) Date for submission of the Recipient's final technical and cost and pricing proposal: No later than (NLT) Monday, June 12, 2020.

(b) Date for start of negotiations: NLT Monday, June 22, 2020.

(c) Target date for definitization: NLT August 1, 2020 (75 days after the date of the Advanced Agreement and shall not exceed $413,200,000.00). The Government anticipates adding up to $786,800,000 when the contract is definitized, for a total Other Transaction Agreements value of $1,200,000,000.

III. SPECIAL PROVISIONS

A. EXECUTION AND COMMENCEMENT OF WORK

The Recipient shall indicate acceptance of this Advanced Agreement by signing the agreement and returning it to the Other Transactions Agreement Officer (OTAO) (referred to throughout as the "OTAO"). Upon acceptance by both parties, the Recipient shall proceed with performance of the work, including purchase of necessary material.

B. DEFINITIZATION AND LIMITATION ON GOVERNMENT LIABILITY

(a) An Other Transaction Authority (OTA) definitive agreement will follow NLT August 1, 2020. The Recipient agrees to negotiate the terms of the definitive agreement that will include mutually agreeable terms and conditions. The Recipient agrees to submit a detailed Cost Reimbursement proposal NLT Monday, June 12, 2020.

If agreement on definitization of an OTA does not occur by August 1, 2020, and an extension is not granted by the Other Transaction Agreement's Officer (OTAO), the parties agree as follows:

1. Either party can provide a 30 day notice to end this Advanced Agreement.

2. If either party provides the 30 day notice, the parties will negotiate reasonable and necessary terms associated with the termination of the Advanced Agreement. These terms will include, but not be limited to, a full accounting of the status of each aspect of the SOW, the status and completion of deliverables, and agreement on intellectual property rights.

3. At the conclusion of the negotiation, Recipient will provide a final invoice.

Advanced Agreement is in anticipation of Other Transaction Agreement No: 75A501-20-C-00114 between the Department of Health and Human Services and AstraZeneca.

4. The Other Transaction Agreements Officer (OTAO) will evaluate Recipient's final invoice to determine the reasonableness of the costs invoiced. Cost will be evaluated in accordance with Generally Accepted Accounting Principles, historical data, and other identified information.

5. The OTAO's reasonableness determination is subject to Recipient appeal to the Head of Contracting Activity and other remedies to the extent permitted by law.

(c) To the extent consistent with this section, all clauses, terms, and conditions included in this Advanced Agreement shall continue and upon the execution of an Other Transaction Agreement, except those that by their nature apply only to an Advanced Agreement.

(d) The Recipient must comply with the principles set forth as follows to gain Government reimbursed costs.

C. OBLIGATION AND PAYMENT

(a) Obligation

The Government's liability to make payments to the Recipient is limited to only those funds obligated pursuant to this Advanced Agreement.

(b) Payments

The Recipient has an established and agrees to maintain an accounting system, which complies with Generally Accepted Accounting Principles and the requirements of this Advanced Agreement, and shall ensure that appropriate arrangements have been made for receiving, distributing and accounting for Federal funds. An acceptable accounting system is one in which all costs, cash receipts and disbursements for which Recipient is entitled to reimbursement are controlled and documented properly. The Recipient will invoice the Government b(4) . The Recipient's costs incurred during the reporting period shall be reported in the Financial Status Report and b(4) . The Recipient properly prepared invoice(s) will be submitted for payment b(4) in Adobe Acrobat (.pdf) format. The invoice shall be uploaded to a shared electronic file server, with an email copy to the OTAO, OTAS and OTTR cited below. As directed by the OTAO, the invoice shall be accompanied by adequate documentation to support the payment. After verification of the accomplishment of the work for which reimbursement is sought by the OTAO, the OTAS and OTTR will forward the invoice(s) to the Program Support Center (PSC). Each invoice must contain the following information in order to be deemed properly prepared:

i. Name and address of Recipient
ii. Invoice Date and Invoice Number
iii. Agreement Number
iv. Description, quantity, unit of measure, unit price, and extended price

Advanced Agreement is in anticipation of Other Transaction Agreement No: 75A501-20-C-00114 between the Department of Health and Human Services and AstraZeneca.

v. Recipient Cost Share
vi. Name and address of OTAR official to whom voucher is to be sent
vii. Name, title, phone number, and mailing address of person to notify in the event of a defective invoice.
viii. Taxpayer Identification Number (TIN)
ix. Electronic funds transfer (EFT) banking information.

Documents should be delivered electronically to the OTAO, OTAS, OTTR, PSC, and e-room electronically. Unless otherwise specified by the OTAO all deliverables and reports furnished to the Government under the resultant Agreement (including invoices) shall be addressed as follows:

NAME Francine Hemphill (OTAO) Francine.Hemphill@acf.hhs.gov and Donna Brockington (OTAS) Donna.Brockington@hhs.gov HHS/ASPR/BARDA 330 Independence Avenue, S.W., Room G640 Washington, DC 20201 Email: Name@hhs.gov	NAME David Simon (OTTR) David.Simon@hhs.gov HHS/ASPR/BARDA 330 Independence Avenue, S.W., Room G640 Washington, DC 20201 Email: Name@hhs.gov	Email invoices to: PSC_Invoices@psc.hhs.gov and E-Room: Link: https://eroom.bardatools.hhs.gov/eRoom

b(4) invoices must include the cumulative total costs submitted for reimbursement to date, adjusted (as applicable) to show any amounts suspended by the Government.

The Recipient will convert foreign currency costs to US dollars b(4) using the closing spot exchange rate published by Reuters on the last working day of each month at: http://www.reuters.com/finance/currencies/quote?srcAmt=1.00&srcCurr=GBP&destAmt=&destCurr=USD

The Recipient agrees to promptly notify the OTAO and OTTR in writing if there is an anticipated overrun (any amount) or expended b(4) of the obligated funds for the base segment or any option segment(s) and the reasons for the variance.

The Government will pay in US dollars all proper invoices within 30 days of receipt or pay interest on any amounts due in accordance with the Prompt Payment Act.

(c) Limitation of Payments

Advanced Agreement is in anticipation of Other Transaction Agreement No: 75A501-20-C-00114 between the Department of Health and Human Services and AstraZeneca.

It is herein understood and agreed that Government funds are to be used solely for this Advanced Agreement and must be reasonable in nature and amount. The following cost principles are effective under this Advanced Agreement for determining the allowability of costs for which reimbursement is sought under this Agreement. b(4) .

Allocability shall be determined in accordance with the standards set forth in FAR § 31.201-4. The Cost Accounting Standards do not apply to the Recipient or any SubRecipient. Costs shall be accounted for in accordance with the Recipient's or SubRecipient's commercial accounting practices.

To be reasonable, a cost must: be generally recognized as an ordinary or necessary part of the business; follow sound business practices; follow what a prudent business person would accept; comply with federal, state, and local laws; and be consistent with the Recipient's or SubRecipient's established practices.

In addition, Recipient's costs that are passed onto the Government for reimbursement shall comply with the procedures and cost principles set forth herein and subsequent other transaction agreement.

The cost principles set forth in subparagraphs (a) shall only apply to the reimbursement of direct costs under cost-type SubAgreements. b(4)

(d) Financial Records and Reports

As directed by the OTAO, the Recipient shall maintain adequate records to account for all funding under this Agreement and shall maintain adequate records to account for Recipient funding provided under this Agreement in support of the Financial Status. Upon completion of the Advanced Agreement or subsequent agreement, whichever occurs latest, the Recipient Administrator shall furnish to the OTAO a copy of the financial report that will be outlined in the subsequent agreement. The Recipient's relevant financial records are subject to examination or audit on behalf of HHS by the Government for a period not to exceed b(4) b(4) after expiration of the Other Transaction Agreement contemplated by this Advanced Agreement, whichever is later. The OTAO or designee shall have direct access to sufficient records and information of the Recipient, to ensure full accountability for all amounts reimbursed by HHS under this Advanced Agreement and the Other Transaction Agreement contemplated by 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.

D. INTELLECTUAL PROPERTY RIGHTS

b(4)

Advanced Agreement is in anticipation of Other Transaction Agreement No: 75A501-20-C-00114 between the Department of Health and Human Services and AstraZeneca.

b(4)

E. PRIORITIES AND ALLOCATIONS AUTHORITY

HHS reserves the right to exercise priorities and allocations authority with respect to this Advanced Agreement and resultant OTA, to include rating this order in accordance with 45 CFR Part 101, Subpart A—Health Resources Priorities and Allocations System at no additional cost to the USG.

IV. STATEMENT OF WORK (SOW) AND DELIVERABLES

WBS 1 Technology Transfer to Enable Large Scale Manufacturing

1. Objectives

a. Drug Substance (DS) and Drug Product (DP) process development for the ChAdOx1 COVID-19 vaccine candidate, scale-up and characterization
b. Development of a multidose preparation will be performed
c. PPQ for both DS and DP will be executed
d. Stability study program executed and maintained for the life of the contract
e. Studies to enable launch and support licensure will be assessed and executed as appropriate.

2. Deliverables

a. Technology Transfer Protocol
b. Method qualification report(s)
c. Method validation report(s)
d. Process Validation Master Plan
e. PPQ report(s)
f. Stability report(s)
g. Comparability report

WBS 2 Drug Substance Manufacturing

1. Objectives

AstraZeneca will oversee, review and approve and release of drug substance at a designated SubRecipient as identified and agreed upon by BARDA and AstraZeneca to complete the objective of manufacturing drug substance to meet the b(4) doses target.

2. Deliverables

a. Certificates of Analysis
b. Stability study plan

Advanced Agreement is in anticipation of Other Transaction Agreement No: 75A501-20-C-00114 between the Department of Health and Human Services and AstraZeneca.

c. Shipping study protocol
d. Shipping study report
e. Executed Quality/Material Transfer Agreements (QA/ MTA).

WBS 3 Drug Product Manufacturing

1. Objectives

AstraZeneca will oversee, review and approve and release of drug product at either a designated SubRecipient or internal AstraZeneca facility identified by AstraZeneca with the objective of producing up to approximately b(4) doses. b(4)

2. Deliverables

a. Manufacturing batch production records for final drug product
b. Executed Quality/Material Transfer Agreements (QA/ MTA).

WBS 4 Pack and Label of Filled Product

1. Objectives

a. Labeling and bulk packing of vials
b. Preparation of finished product on pallets ready to ship
c. Storage of finished product up to b(4)

2. Deliverables

a. Final drug product release reports
b. Manufacturing batch production records for final drug product

WBS 5 Reproductive Toxicology

1. Objectives

Perform developmental and reproductive toxicology study

2. Deliverables

Study report

WBS 6 Phase 3 Clinical Study in Adults

1. Objectives

Advanced Agreement is in anticipation of Other Transaction Agreement No: 75A501-20-C-00114 between the Department of Health and Human Services and AstraZeneca.

Develop and protocol and perform a Phase 3 pivotal randomized, placebo-controlled efficacy study in adults 18+ years of age to demonstrate protection against confirmed COVID-19. Feedback and input from the FDA is expected (The sample size for the trial is expected to be b(4) subjects with a 2:1 ratio of vaccine to placebo). AstraZeneca may begin working with the NIH network immediately upon signing the Advanced Agreement.

2. Deliverables

a. Study synopsis
b. Study protocol
c. Interim reports
d. Draft and final Clinical Study report

WBS 7 Phase 3 Pediatric Study

1. Objectives

a. Develop a clinical protocol based on FDA feedback (The sample size for the trial is expected to be b(4) subjects with a 2:1 ratio of vaccine to placebo)
b. Based on FDA feedback, perform a randomized, placebo-controlled efficacy study in children 17 years of age or less to demonstrate protection against confirmed COVID-19.

2. Deliverables

a. Study synopsis
b. Study protocol
c. Interim reports
d. Draft and final Clinical Study report

WBS 8 Regulatory Support

1. Objectives

a. Activities to support an IND for the ChAdOX1 COVID-19 vaccine

b. Preparation of regulatory documentation associated with an EUA for vaccine deployment
c. BLA preparation and submission

2. Deliverables

a. Draft and final Regulatory minutes
b. Draft and final Regulatory submissions

Advanced Agreement is in anticipation of Other Transaction Agreement No: 75A501-20-C-00114 between the Department of Health and Human Services and AstraZeneca.

WBS 9 Project Management

1. **Activities**

   a. All project management activities associated with the clinical development and manufacturing of ChAdOx1 COVID-19 vaccine.
   b. OTA close out report

2. **Deliverables**

   a. Recipient should provide an Integrated Master Schedule, which includes WBS, critical path and milestones within b(4) of Advanced Agreement execution. This should be updated over time at the request of the Government.
   b. A teleconference call between the Other Transaction Technical Representative and the Recipient's Program Manager shall occur bi-weekly (every two weeks), or at the discretion of the Government. During this call, the Program Manager will discuss the activities during the reporting period, any problems that have arisen, and the activities planned for the ensuing reporting period. The Recipient's Program Manager may choose to include other key personnel on the conference call to give detailed updates on specific projects or this may be requested by the Other Transaction Agreement's Representative.
   c. The Recipient shall participate in Project Meetings to coordinate the performance of the OTA, as requested by the Other Transaction Technical Representative. These meetings may include teleconferences, face-to-face meetings with the OTTR and the OTAO in Washington, D.C. and at work sites of the Recipient and its SubRecipients. Such meetings may include, but are not limited to, meetings of the Recipient (and SubRecipients invited by the Recipient) to discuss b(4) . The Recipient shall provide data, reports, and presentations to groups of outside experts (subject to appropriate protections for Recipient confidential or proprietary data) and USG personnel as required by the Other Transaction Technical Representative in order to facilitate review of OTA activities.
   d. Upon request, Recipient shall provide OTAO and OTTR with deliverables from the following OTA funded activities b(4) .
   e. The Recipient shall memorialize any correspondence between Recipient and FDA and submit to the OTAO and OTTR. All documents shall be duly marked as either "Draft" or "Final". The Recipient shall forward the dates and times of any meeting with the FDA to the OTAO and OTTR and make arrangements for appropriate government staff to attend the FDA meetings. Government staff shall include up to a maximum of four people OTAO up to 2 subject matter experts).

f. In the event of an FDA inspection, which occurs because of this agreement and for the product, or for any other FDA inspection that has the reasonable potential to impact the performance of this OTA, the Recipient shall provide the Government with an exact copy (non-redacted) of the FDA Form 483 and the Establishment Inspection Report (EIR). The Recipient shall provide the OTAO and OTTR with copies of the plan for addressing areas of nonconformance to FDA regulations for GLP, GMP, or GCP guidelines as identified in the audit report, status updates during the plans execution and a copy of all final responses to the FDA. The Recipient shall also provide redacted copies of any FDA audits received from SubRecipients that occur because of this OTA or for this product. The Recipient shall make arrangements for BARDA representative(s) to be present during the final debrief by the regulatory inspector.

g. BARDA Quality group and /or their qualified representatives reserves the right to participate in QA audits. Upon completion of the audit/site visit the Recipient shall provide a report capturing the findings, results and next steps in proceeding with the SubRecipient. If action is requested of the SubRecipient, detailed concerns for addressing areas of nonconformance to FDA regulations for GLP, GMP, or GCP guidelines, as identified in the audit report, must be provided to the OTAO and OTTR. The Recipient shall provide responses from the SubRecipients to address these concerns and plans for corrective action execution.
    1) Recipient shall notify the OTAO and OTTR b(4) in advance of upcoming, ongoing, or recent audits/site visits of SubRecipients as part of b(4) communications.
    2) Recipient shall notify the OTAO and OTTR within b(4) of report completion.
    3) If issues are identified during the audit, the Recipient shall submit a report to the OTAO and OTTR within:
        - b(4) detailing the finding and corrective action(s) of the audit.
        - OTAO and OTTR will review the report and provide a response to the Recipient within b(4).
        - Once corrective action is completed, the Recipient will provide a final report to the OTAO and OTTR.

h. Recipient shall also accommodate any 'for cause' audit if and when there are potential issues identified in the program during the period of performance. Such issues include but are not limited to stability failures, GLP issues etc. If the OTAO, OTTR, Recipient, or other parties identifies any issues during an audit, the Recipient shall capture the issues, identify potential solutions, and provide a report to the OTAO and OTTR.
    - If issues are identified during the audit, Recipient shall submit a report to the OTAO and OTTR detailing the finding and corrective action(s) within b(4) of the audit.

i. OTA Close Out Report

3. Special Contract Requirement

Advanced Agreement is in anticipation of Other Transaction Agreement No: 75A501-20-C-00114 between the Department of Health and Human Services and AstraZeneca.

AstraZeneca, or any entity or representative acting on behalf of AstraZeneca, may not refer to this Advanced Agreement or work/services furnished pursuant to the provisions of this Advanced Agreement or resulting OTA in any news release or commercial advertising, or in connection with any news release or commercial advertising, without first obtaining explicit written consent to do so from the OTAO or the HHS Press Office.

At the time of signature on this Advanced Agreement, AstraZeneca shall provide the name and contact information for a point of contact for a representative from its Press Office.

Should any reference to this Advance Agreement or OTA be included in any news release or commercial advertising issued by or on behalf of AstraZeneca without the required written consent, the Government will consider the institution of all remedies available under applicable law.

VI. ADMINISTRATION:

Requisition Number: OS259266

A. The sums to be expended by the Government hereunder are chargeable to the following allotments, the available balances of which are sufficient to cover the same:

2020.199C001.25103	$ 413,200,000.00.
(fund citation)	(amount)

B. The overall administrative responsibility for this OTA lies with OTAO and OTTR.

C. Payments will be made by the Program Support Center (PSC) by submitting invoices to PSC_invoices@psc.hhs.gov (CMA Administering Other Transaction Agreements and Other Transaction Technical Representative shall also be copied in submission email)

Type of contract contemplated: OTA

This instrument has been negotiated pursuant to Section 247d-7e (c)(4)(B) of Title 42 U.S. Code.

b(6)

May 20, 2020
Date

AstraZeneca Pharmaceuticals LP
1800 Concord Pike
Wilmington, DE 19803

Francine L. Hemphill
Other Transaction Agreements Officer

May 20, 2020
Date

DEPARTMENT OF HEALTH AND HUMAN SERVICES
ADVANCED AGREEMENT BETWEEN THE ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE (ASPR), BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY (BARDA)
AND
ASTRAZENECA
OTHER TRANSACTION AGREEMENT NUMBER: 75A501-20-C-00114 MOD P00001
TITLE FOR: ChAdOx1nCoV-19 Vaccine Clinical Development and Manufacturing

The purpose of this modification is to update the target date of definitization of the Other Transaction Agreement (OTA)

Modification of subject Advanced Agreement to be as follows:

FROM:

II. DEFINITIZATION SCHEDULE

(a) Date for submission of the Recipient final technical and cost and pricing proposal: No later than (NLT) Monday, June 12, 2020.
(b) Date for start of negotiations: NLT Monday, June 22, 2020.
(c) Target date for definitization: NLT August 1, 2020 (75 days after the date of the Advanced Agreement and shall not exceed $413,200,000.00). The Government anticipates adding up to $786,800,000 when the contract is definitized, for a total Other Transaction Agreements value of $1,200,000,000.

TO:

II. DEFINITIZATION SCHEDULE

(a) Date for submission of the Recipient final technical and cost and pricing proposal: No later than (NLT) Monday, June 12, 2020.
(b) Date for start of negotiations: NLT Monday, June 22, 2020.
(c) Target date for definitization: NLT August 31, 2020 (105 days after the date of the Advanced Agreement and shall not exceed $413,200,000.00). The Government anticipates adding up to $786,800,000 when the contract is definitized, for a total Other Transaction Agreements value of $1,200,000,000.

This instrument has been negotiated pursuant to Section 247d-7e (c)(4)(B) of Title 42 U.S. Code

There are no other changes to Terms and Conditions of this Agreement

(b) (6)

Ruud Dobber, PhD
EVP and President,
BioPharmaceuticals Business Unit
AstraZeneca Pharmaceuticals LP
1800 Concord Pike
Wilmington, DE 19803

July 31, 2020

(Date)

07/31/2010

Francine Hemphill
Other Transaction Agreement's Officer