I S T C

М Н Т Ц

PROJECT AGREEMENT #G-1759p

BETWEEN

THE INTERNATIONAL SCIENCE AND TECHNOLOGY CENTER,

THE NATIONAL CENTER FOR DISEASE CONTROL AND PUBLIC HEALTH AND

THE DEPARTMENT OF HEALTH AND HUMAN SERVICES OF THE UNITED STATES OF AMERICA

Epidemiology of *Clostridium difficile*-associated disease in Georgia

Operative Commencement Date: Decemder 1, 2013

Definitions
"Agreement" means an ISTC project agreement
"Party" means a Party to the Agreement Establishing an International Science and Technology Center
"Financing Party" means a Party providing funds for an ISTC project (The United States Department of Health and Human Services through the BTEP program);
"Partner" means an organization that has been approved by the ISTC Governing Board to participate in the ISTC Partner Program on a regular basis (The U.S. Department of Health and Human Services) and acts as an ISTC partner;
"Recipient" means an organization of the Russian Federation or other country of the former Soviet Union, which conducts work under an ISTC project agreement

The International Science and Technology Center (hereinafter referred to as "**the Center**"), **the National Center for Disease Control and Public Health** (hereinafter referred to as "**the Recipient**"), and **the U.S. Department of Health and Human Services** (hereinafter referred to as the "**Partner**"), represented for the purpose of the signature of this Project Agreement (hereinafter referred to as "**the Agreement**") by their authorized representatives (with the Center, the Recipient, and the Partner hereinafter referred to collectively as "**the Signatory Parties**"),

TAKING INTO ACCOUNT THE FOLLOWING CONSIDERATIONS:

The United States of America, Japan, the Russian Federation and, acting as one Party, the European Atomic Energy Community and the European Community (with these two organizations hereinafter referred to as "**the European Community**") signed the Agreement Establishing the International Science and Technology Center on November 27, 1992 (hereinafter referred to as "**the ISTC Agreement**") and the Protocol on Provisional Application of the Agreement Establishing the International Science and Technology Center on December 27, 1993 (hereinafter referred to as "**the ISTC Protocol**"),

The Republic of Georgia, the Republic of Armenia, the Republic of Belarus, the Republic of Kazakstan, the Kyrgyz Republic, Norway, the Republic of Korea, the Republic of Tajikistan and Canada have acceded, and additional States may accede, to the ISTC Agreement and to the ISTC Protocol to participate in the activities of the Center,

The Center is a legal entity and has been registered by the Ministry of Foreign Affairs of the Russian Federation as an international organization with its headquarters in Moscow,

The Recipient is a legal entity within the Republic of Georgia,

The Partner, established as a U.S. Federal Department under U.S. law and having its principal office in Washington, DC, is a legal entity that has been approved by the Center's Governing Board to participate in Center activities as an ISTC Partner, in accordance with the Memorandum of Agreement between ISTC and DHHS signed on July 6, 1999 and August 10,1999.

The Governing Board of the Center has approved a project to be funded by the Partner through the Center in the domain covered by the Agreement concerning cooperation in approved projects in the health sector to facilitate the non-proliferation of weapons and weapons expertise.

The Partner has agreed to provide financial support for such project, under the DHHS Biotechnology Engagement Program (BTEP) and in accordance with the Article II, paragraph 2 of the Memorandum of Agreement.

As set forth in the ISTC Agreement, funds received by a legal entity in connection with the Center's projects shall be excluded in determining the profits of that organization for the purpose of tax liability and funds received by persons in connection with the Center's projects shall not be included in these persons' taxable incomes,

All parties to this Project Agreement shall conduct this project of work consistent with the principles of the ISTC Statute provisions and applicable international conventions and agreements for which the USA and Republic of Georgia are Parties.

HAVE AGREED AS FOLLOWS:

Article 1 - Scope of the Agreement

1.1 The Recipient shall carry out the work plan set forth in Annex I according to the conditions of the Agreement, subject to the provisions of the ISTC Agreement, the ISTC Protocol, the Statute of the Center (hereinafter referred to as "the ISTC Statute"), and the Principles for Partner Participation in ISTC Activities, which govern in case of conflict. The activities carried out under the Agreement are entitled: *Epidemiology of Clostridium difficile-associated disease in Georgia* – **(hereinafter referred to as "the Project").**

1.2 Subject to any special conditions in Article 11 or any amendments or exclusions by any other Articles, the detailed terms of the Agreement are specified in the Annexes that form an integral part of the Agreement. In the case of conflict between any provision in the Annexes and any other provision of the Agreement, the latter shall prevail.

1.3 The Partner may request through the Center access to the Project site for the consultation on and the evaluation of the progress of the Project. The Recipient shall use its best efforts to comply with such requests.

Article 2 - Duration of the Project

The duration of the Project is estimated to be 18 months from December 1, 2013 (hereinafter referred to as "**the Operative Commencement Date**").

Article 3 - Sub-agreements with Other Participating Institutions

There are no sub-agreements relating to the Agreement.

Article 4 - Financial Contribution of the Partner through the Center

4.1 The total cost of the Project to the Center shall not exceed US$ 100,000.00 (One hundred thousand dollars and zero cents). This total includes:

(1) items to be reimbursed in cash to the Recipient in accordance with Article 4.3,
(2) grants in cash to be made by the Center directly to the individual participants in the Project (hereinafter referred to as "**Individual Participants**") for financial support of the Individual Participants in accordance with Article 4.4, and
(3) items to be provided in-kind by the Center to the Recipient in accordance with Article 4.5.

After further consideration of the costs and availability of the items to be provided, the Recipient may, with the concurrence of the Center's representative, interchange items between Articles 4.3 and 4.5 with corresponding adjustments of the cost estimates for each Article.

4.2 The Partner shall provide to the Center project funds consistent with the bilateral financial Memorandum of Agreement between the Center and the Partner no later than the Operative Commencement Date of the Project.

4.3 The Center shall reimburse the Recipient for expenditures by the Recipient in accordance with Annexes I and II. The estimated cost of such expenditures is US$4,580.

4.4 The Center shall make direct grants in dollars to Individual Participants in the Project in accordance with Annex I at an estimated cost of US$59,595. This amount can be increased at the request of the Recipient and with the concurrence of the Center's representative and of the affected Individual Participants provided the costs of Article 4.3 and/or Article 4.5 are reduced accordingly.

4.5 The Center's in-kind contributions to the Recipient are estimated at US$35,825. These in-kind contributions will be provided in accordance with the lists of items to be provided and the timetables set forth in Annex I in order to enable the Recipient to meet the work schedule for the Project. Failure by the Center to provide the in-kind contributions in a timely manner may give rise to a modification of the relevant provisions of the Agreement.

The Center's in-kind contributions, which are provided for exclusive use on the Project by the Recipient during the lifetime of the Project, include the following categories of items:

4.5.1 The Center shall provide in-kind equipment to the Recipient (if any) in accordance with Annex I (hereinafter referred to as "**Center Provided Equipment**"). Center Provided Equipment will be delivered to the Recipient at a CIS customs entry point specified by the Center. The Center will be responsible for clearance through customs, and the Recipient will be responsible for transporting the equipment from the customs entry point to the site of the Project. The equipment shall be inventoried, preserved, accounted for, and maintained throughout the Project by the Recipient. The equipment shall be used only in areas that are open for monitoring and auditing in accordance with Article 9. The title to Center Provided Equipment with an acquisition per item cost of less that $2,500 will vest in the Recipient once it has been provided. The title to all other Partner Provided Equipment will remain with the Center, unless mutually agreed otherwise.

4.5.2 The Center shall provide in-kind materials in accordance with Annex I (hereinafter referred to as "**Center Provided Materials**"). Center Provided Materials will be delivered to the Recipient at a CIS customs entry point specified by the Center. The Center will be responsible for customs clearance, and the Recipient will be responsible for transporting the materials to the site of the Project.

4.5.3 The Center shall provide in-kind services (if any) in accordance with Annex I (hereinafter referred to as "**Center Provided Services**").

4.5.4 The Center shall provide in-kind international travel by the Recipient in accordance with Annex I (hereinafter referred to as "**Center Provided Travel**"). The cost of the Center's contribution will not exceed US$11,900.

Center Provided Travel will be undertaken by participants in the Project only after advance approval for each trip by the Partner and notification to the Center. The Recipient shall send to the Partner and Center requests for travel not less than 30 days prior to the beginning of each trip unless a shorter time for advance request is approved by the Partner and then by the Center for a specific trip. The Center will provide directly to the traveler the funds to cover such travel, provided that such travel is approved by the Partner prior to the beginning of the travel.

The Center's responsibility does not include making arrangements for visits, passports, visas, or travel reservations but is limited to providing financial support, including funds to cover the costs of passport and visa fees as well as transportation and lodging, in accordance with the travel regulations of the Center.

The Recipient is responsible for ensuring that the financial support requested pursuant to this paragraph does not exceed the financial limit set forth above.

4.5.5 The Center shall provide in-kind the costs of certain bank transfer fees in accordance with Annex I (hereinafter referred to as "**Center Provided Bank Fees**"). They will be limited to fees necessary to transfer funds into the bank account or accounts of the Recipient and fees associated with the payment of cash to Individual Participants in the Project. They will be paid directly by the Center to the appropriate banks.

Article 5 - Cash Payments by the Center to the Recipient

5.1 Pursuant to Article 4.2, the Center shall make its payments to the Recipient through Dedicated Bank Account(s), as set forth in Article 6. 6 of Annex II in banks acceptable to the Center.

- An advance payment of US$1,330 which is the estimated level of expenditures by the Recipient during the first six months of the Project, as soon as possible following the Operative Commencement Date;
- Quarterly payments within one month of the receipt by the Partner and Center of progress or annual reports and associated cost statements in accordance with Article 7 and Annexes II and III. The amounts of the payments shall be estimates by the Center of the funds required to support the work plan set forth in Annex I during each of the succeeding quarters taking into account the cost statement from the previous period;
- A retention shall be made by the Center of US$3,000. The retention shall be released to the Recipient within one month following the approval by the Partner and Center of the last technical or financial document or other deliverable required by the Agreement.

5.2 Pursuant to Article 4.4, the Center shall make grant payments directly to Individual Participants in accordance with letters of agreement between the Center and the Individual Participants. The Center shall ensure that banking arrangements are established for these payments.

At the end of the third month following the Operative Commencement Date and every three months thereafter throughout the duration of the Project, the Recipient represented by the Project Manager who is identified in Annex I will provide the Partner and the Center with a list of grant payments that are due at that time to Individual Participants in accordance with the payment levels set forth in Annex I and the amount of time devoted to the Project by each Individual Participant as certified by the Project Manager. Such payments will then be promptly made as appropriate by the Center.

Since the Individual Participants will remain employees of the Recipient, the Center's act of direct grant payments to the Individual Participants will not transfer from the Recipient to the Partner or the Center any liability for damages caused by the Individual Participants during execution of the Projects or any liability for damages to the Individual Participants during execution of the Project.

Article 6 - Cost Statements by the Recipient

6.1 Quarterly cost statements shall be submitted by the Recipient to the Partner and the Center as follows:

To the Center, the Partner and the U.S. Counterpart Scientist:
– English: one copy via electronic transmission (e-mail or on diskette) and one printed copy;

The first statement is to be submitted no later than four months after the Operative Commencement Date and will cover the first three months of Project activity. Subsequent statements are to be submitted at three-month intervals following submission of the first statement. The statements will be appended to the relevant technical reports specified in Article 7. The cost statements will include the costs of grant payments directly to Individual Participants, but the requests for such grant payments in accordance with Article 5 should not be delayed pending preparation of the entire quarterly cost statements called for in this Article. Such payments may be nevertheless suspended by the Center in case if the cost statement for the previous quarter was not yet submitted to the Center.

6.2 A consolidated cost statement shall be submitted by the Recipient to the Partner and the Center within two months of the completion, cessation or termination of the work financed by the Partner as follows:

To the Center, the Partner and the U.S. Counterpart Scientist:
– English: one copy via electronic transmission (e-mail or on diskette) and one printed copy;

If such a statement is not submitted on time, the Center or the Partner may request in writing its submission. If the Center and the Partner do not receive the submission within thirty days after such a written request, the Center, in consultation with the Partner, may consider the previously claimed costs to be final and determine to make no further reimbursement.

6.3 Cost statements shall comply with the formats prescribed in Annex III.

Article 7 - Reports and Other Project Outputs

7.1 The Recipient shall submit the following reports in accordance with the format prescribed in Annex III as follows:
To the Center, the Partner and the U.S. Counterpart Scientist:
– English: one copy via electronic transmission (e-mail or on diskette) and one printed copy;

It is the responsibility of the Recipient, in consultation with the Partner, to indicate clearly what parts of reports and other project outputs contain invention or business confidential information and specify any limitations on circulation. For each report or other project output, an unrestricted version shall also be provided. All reports containing invention or business confidential information shall be handled by the Center according to established internal procedures.

- Quarterly progress reports covering each three-month period following the Operative Commencement Date to be submitted within one month after the end of each reporting period.

- Annual reports. For projects of duration of more than one year, an annual report will be submitted 13 months after the Operative Commencement Date and will cover the first year of project activity. For projects of duration of more than two years, a second annual report will be submitted 12 months later.

- Other reports. The Recipient and the Partner will define other reports in Annex I.

- A final report. A draft final report will be submitted to the Center and the Partner within two months of the completion of the Project work plan, cessation or termination of the Agreement, or the agreed completion date of the Agreement, whichever is the earliest. The Partner, in consultation with the Center, shall submit to the Center and Recipient its evaluation and comments on the draft final report within two months after receipt of the latter. The definitive final report will then be submitted by the Recipient to the Center and the Partner within one month after receipt of the Partner's evaluation. If the Partner does not submit an evaluation within two month, the draft final report shall be considered the definitive final report.

- Edited reports for publication will be provided as specified in Article 4.1 (c) of ANNEX II.

7.2 For the purposes of the Agreement, "deliverables" are defined as any significant outputs, including all reports, of the Project to be submitted in accordance with Annexes I, II and III.

Article 8 - Ownership and Exploitation of Results

8.1 The results arising from the Agreement shall be allocated between the Recipient and the Partner in accordance with Part E of Annex II. The Recipient and the Partner shall take appropriate action to exploit or commercialize the results and to make available the results to third parties in accordance with the framework specified in Part E of Annex II. Cooperation agreements with foreign institutions complementing, but not conflicting with, this Framework may be entered into by the Recipient and the Partner.

8.2 Prior to completion of the Project, the Recipient shall submit to the Center a Technology Implementation Plan developed in consultation with the Partner. For projects with a duration of eighteen months or longer, this Plan will be submitted 6 months prior to the anticipated Project completion date. For projects with a duration of less than eighteen months, the Plan will be submitted three months prior to the anticipated Project completion date.

8.3 Exploitation of results shall be limited to applications for peaceful purposes. In this regard, the Recipient and the Partner shall ensure that any results which could result in concerns over proliferation of weapons technology and transfer of sensitive technologies will be protected in accordance with relevant laws of the Republic of Georgia and international agreements and conventions to which the Republic of Georgia is a Party.

Article 9 - Auditing and Monitoring

9.1 Access by the Center to carry out on-site monitoring of all technical activities of the Project shall be granted by the Recipient, and information and assistance shall be given for the verification and evaluation of the Project activities as set out in Annex II.

9.2 Financial audits of costs may be carried out by the Center as specified in Annex II.

9.3 Auditing and Monitoring of institutions located in closed cities shall be carried out according to the procedures adopted at the sixth Governing Board Meeting of the Center.

Article 10 - Amendments, Variations, or Additions

The provisions of this Agreement and its Annexes may be amended or supplemented only by means of a written agreement signed by authorized representatives of the Signatory Parties. However, operational changes in Annex I, other than changes in the Project Manager, the Participating Institution, daily rates of leading persons of the Project and the overall schedule, can be made by agreement between the Center and the Recipient.

Article 11 - Special Conditions

11.1 With respect to the Protection of Human Subjects

(i) The CDC has reviewed the proposed activities and found that they do consist of research involving human subjects.

(ii) The project proposal must be reviewed in accordance with the U.S. law and international policies and regulations regarding biomedical research involving human subjects

(iii) The Implementing Agencies shall be responsible for ensuring that any research work conducted under this project Agreement shall be carried out consistent with The Public Health Service Act as Amended by the Health Research Extension Act of 1985 and the Federal Policy for the Protection of Human Subjects of 1991

(iv) The Recipient and the Partner shall follow the principles of *The Belmont Report, Principles and Guidelines for Protection of Human Subjects of Research* or *The World Medical Association Declaration of Helsinki, Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects*, adopted by the 18th World Medical Assembly and revised in 1989.

11.2 With respect to the use of Laboratory Animals

(i) Laboratory animals and/or endangered species are not expected to be a subject of this research or be involved during the execution of work under this specific project.

(ii) However, if this proves otherwise, the project proposal must be reviewed in accordance with the U.S. law and international policies and regulations regarding biomedical research involving laboratory animals

(iii) The Implementing Agencies shall be responsible for ensuring that any activity carried out pursuant to this agreement and involving laboratory animals is in compliance with the Foreign State of Compliance, International Guiding Principles for Biomedical Research and the Public Health Service Policy on Humane Care and Use of Laboratory Animals as revised in September of 1986

11.3 With respect to transport of Biological Samples

Any export/import involving transportation of biological samples shall be conducted in accordance with the existing laws, regulations, and administrative procedures of the United States of America and the Republic of Georgia. For current information regarding this issue please contact the following:

(i) For U.S. exports: Department of Commerce, Bureau of Export Administration at (202) 482-4811.

(ii) For U.S. imports of etiologic agents of humans: Centers for Disease Control and Prevention, Office of Health and Safety at (404) 639-2453.

(iii) For U.S. imports of etiologic agents of livestock, poultry and other animals: United States Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services at (301) 734-3277.

11.4 With respect to Manipulation of Genetic Material through the Use of Recombinant DNA Techniques

(i) The CDC has reviewed the proposed activities and found that they do not consist of research involving recombinant DNA techniques for genetic manipulation.

(ii) However, if this proves otherwise, the project proposal must be reviewed in accordance with applicable U.S. law and international policies and regulations, including the current "NIH Guidelines for Research Involving Recombinant DNA Molecules." These guidelines can be found on the NIH website at http://www.nih.gov/od/oba or from the NIH Office of Recombinant DNA Activities (301-496-9838).

(iii) The BTEP Advisory Group may ask the investigators to initiate a review by the appropriate Recombinant DNA Advisory Committee (RAC) or Institutional Biosafety Committee (IBC) at any time.

Article 12 - Disputes

Disputes arising during performance of this Agreement including, in particular:
(i) A claim by the Recipient for any payments deemed due;
(ii) An interpretation of a provision of the Agreement; or
(iii) A request for relief or approval related to the Agreement,

shall be subject to the following procedure:

The Recipient shall submit any claim, demand, or request in writing to the Partner and to the Center. The Partner and the Center will prepare a joint response. Unless a longer period is specified in the Agreement, the written decision of the Partner and the Center shall be delivered to the Recipient within four weeks of the receipt of the submission.

Exceptionally, the Recipient may appeal the Partner's and Center's decision in writing through the Executive Director of the Center to the Governing Board of the Center within four weeks of the communication of the Partner's and Center's decision.

The decision of the Governing Board shall be final and binding (unless otherwise provided). Pending the final settlement of disputes, the Recipient shall, nevertheless, proceed diligently with the performance of the Agreement.

Article 13 - Liability

13.1 The Partner and the Center shall not be liable for any material loss, damage, or injury of any nature arising from, or in connection with, the performance of the work under the Agreement solely by virtue of financing the Project, including liability from direct grant payments to Individual Participants as set forth in Article 5.2.

13.2 The Partner and the Center shall not be liable to the Recipient or third parties for claims arising from:

- publication or transmission of any report in accordance with Articles 4 and 13 of Annex II unless it is shown that the Partner or Center have not taken reasonable steps to protect material clearly indicated as invention or business confidential information;
- the application of the contents of any report by a third party; or
- the handling or use of products which result from the Project.

13.3 The Center shall not be liable for nonperformance by the Partner or the Recipient of their obligations under the Agreement.

Article 14 - Suspension and Termination of the Agreement

14.1 Suspension

14.1.1 If the Center identifies a problem with the Project's performance through audit, monitoring, annual reports or other ways, and discussions between the Center and the Recipient which shall ensue pursuant to a notice given by the Center to the Recipient do not produce any results, the Center shall reserve the right to suspend, in consultation with the Partner, the project or, when feasible from technical and other points of view, a part of the Project, within thirty days after the Center issues to the Project Manager a notification of suspension which specifies the problem, the effective date and the period of the suspension. In case auditing and monitoring procedures stipulated in the Agreement and Annex II are breached by the Recipient, the suspension shall come into force ten days after the notification given to the Recipient if no corrective action has been taken during this period.

When the suspension becomes effective, the Center shall pay grants to the individual participants for the period they were engaged in the Project before the Center's declaration of suspension becomes effective. Any other payments or in-kind supplies to the Recipient shall in principle be suspended as long as the suspension remains in effect. The Recipient shall act in due diligence to mitigate any losses which may arise during this period.

Even when the suspension is in effect, the Center and the Recipient shall do the utmost to find a possible solution to the problem.

14.1.2 In case the Center and/or the Partner does not fulfill its obligations arising from the Project, namely in relation to Article 2 and 3, the Recipient shall reserve the right to suspend the Project within thirty days after the Recipient issues to the Executive Director of the Center a notification of suspension which specifies the problem, the effective date and the period of the suspension. Clauses of paragraph three of 14.1.1 shall be applied here as well.

14.2 Termination

14.2.1 When the Project is suspended by the Center, and the period of the suspension which is specified in the Center's notification expires and the Center and the Recipient are unable to find a solution, the Center shall, in consultation with the Partner, terminate the Project. In the event of partial suspension, the Center and the Recipient shall negotiate and agree upon possible measures including partial termination of the Project. If these negotiations do not produce any viable alternative plan, the Center shall reserve the right to terminate the entire Project.

Notwithstanding the termination, the Recipient shall submit reports and cost statements covering the period up to the termination and the following provisions of the Agreement shall continue to apply: Article 12 (Disputes), Paragraph 7 (Accounting Principles, Allowable Costs, and Transfer of Costs) and 8.2 (Equipment) of Annex I of the Agreement, and Part E of Annex II of the Agreement (Information and Intellectual Property).

If the Project is terminated, costs shall be limited to the allowable costs incurred by the Recipient prior to the suspension and other costs which the Center considers to be fair and reasonable having regard to commitments which have been reasonably entered into and which cannot be canceled or avoided.

14.2.2 When the Project is suspended by the Recipient, and the period of the suspension which is specified in the Recipient's notification expires and the Recipient and the Center are unable to find a solution, the Recipient shall terminate the Project. Clauses of paragraphs two and three of 14.2.1 shall be applied here as well.

14.3 Termination by Force Majeure Situations

When Force Majeure situations occur which make the Project implementation impossible, the Center in consultation with the Partner and the Recipient may terminate the Project with application of similar procedures as specified above.

14.4 Termination Forced due to the Violation of Laws or Regulations by the Recipient

When the Recipient has committed actions which obviously violate the national laws of the state where the Recipient is a legal entity or which obviously are contrary to the stated objectives of the Center or to other conditions specified under the ISTC Agreement or the ISTC Statute, the Center shall terminate the Project with immediate effectiveness upon written notification of termination to the Recipient. In this case, the Recipient shall promptly return to the Center all payments and goods previously provided to the Recipient. Notwithstanding any termination, Part E of Annex II of the Agreement will continue to apply.

Article 15 - Correspondence

15.1 Any written notice, request or consent required under the Agreement is deemed to have been given or made when delivered in person to an authorized representative of a Signatory Party or when sent by mail, telex, telegram, electronic mail or facsimile (receipt acknowledgment required) to such Signature Party at the following address:

For the Center:
International Science and Technology Center
32-34 Krasnoproletarskaya Str.,
Moscow 127473, Russia
Facsimile: +7(499)978-4926
Senior Project Manager: Melnikov Vyacheslav

For the Recipient:
National Center for Disease Control and Public Health
9 Asatiani Str, Tbilisi, 0177, Georgia
Facsimile: +995 32 243 30 59
Project Manager: David Tsereteli

For the Partner
U.S. Centers for Disease Control and Prevention
1600 Clifton Road NE, Mailstop A-05
Atlanta, GA 30329, USA
Facsimile: +1(404) 235 0293
BTEP Program Manager: David Bull

For the U.S. Counterpart Scientist:
US Centers for Disease Control and Prevention
1600 Clifton Road
Atlanta, GA 30329, USA
Tel.: +1(404) 639 2882
Associate Director for Food Safety: Dale L. Morse

15.2 Notice will be deemed to be effective as follows:

(i) in the case of personal delivery or mail, on delivery;

(ii) in the case of telexes, telegrams, electronic mail or facsimiles, within one (1) working day following confirmed transmission. A signed original will be provided by mail in all cases.

15.3 Each Signatory Party may change its address for notice hereunder by giving the other Party notice of such change pursuant to this Article.

Article 16 - Annexes

As specified in Article 1.2, the Annexes are an integral part of the Agreement. They are:

Annex I	Work Plan
Annex II	General Conditions
Annex III	Formats for Progress and Cost Reports
Annex IV	Disclaimer

Article 17 - Entry into Force of the Agreement

The Agreement shall enter into force on December 1, 2013.

Prepared in Moscow in the English language.

For the Center	For the Recipient	For the Partner
Leo Owsiacki Executive Director ISTC	Amiran Gamkrelidze General Director National Center for Disease Control and Public Health	David Bull BTEP Program Manager U.S. Centers for Disease Control and Prevention Program (BTEP)
23 Oct 2013	6.11.2013	Nov 18, 2013
(date)	(date)	(date)

ANNEX I

Work Plan

I. Summary Project Information

1. Project Title

Epidemiology of ***Clostridium difficile***-associated disease in Georgia

2. Project Manager

Name: David Tsereteli	
Title: M.D., Ph.D.	**Position:** Chief Researcher
Street address: 9 M. Asatiani str.	
City: Tbilisi	**Region:** Tbilisi
ZIP: 0186	**Country:** Georgia
Tel.: +995 591 40 10 94	**Fax:** +995 32 243 30 59
E-mail: Dr.Tsereteli@gmail.com	

3. Participating Institutions

3.1. Leading Institution

Short reference: NCDC	
Full name: National Center for Disease Control and Public Health	
Street address: 9 M. Asatiani str.	
City: Tbilisi	**Region:** Tbilisi
ZIP: 0186	**Country:** Georgia
Name of Authority: **Signature** Amiran Gamkrelidze	
Title: Prof.	**Position:** Director General
Tel.: +995 32 239 89 46	**Fax:** +995 32 243 30 59
E-mail: a.gamkrelidze@ncdc.ge	
Governmental Agency: Ministry of Labour, Health and Social Affairs of Georgia	

3.2. Other Participating Institutions

None

4. Foreign Collaborators/Partners

4.1. Collaborators

Institution: Centers for Disease Control and Prevention	
Street address: 1600 Clifton Road	
City: Atlanta	**Region/State:** Georgia
ZIP: 30333	**Country:** USA
Person: Dale L. Morse	
Title: MD., MS	**Position:** Associate Director for Food Safety
Tel.: 404-639-2882	**Fax:** -
E-mail: Dym2@cdc.gov	

4.2. Partners

Institution: U.S. Centers for Disease Control and Prevention	
Street address: 1600 Clifton Road NE, Mailstop A-05	
City: Atlanta	**Region/State:** GA
ZIP: 30329	**Country:** USA
Signature Authority: David Bull	
Title: PhD	**Position:** BTEP Program Manager
Tel.: + 1(404) 639-7356	**Fax:** +1(404) 235 0293
E-mail: dbull@cdc.gov	
Project Coordinator: David Bull	
Title: PhD	**Position:** BTEP Program Manager
Tel.: + 1(404) 639-7356	**Fax:** +1(404) 235 0293
E-mail: dbull@cdc.gov	

5. Project Duration

18 months

6. Project Location and Equipment

Institution	Location, Facilities and Equipment
Leading Institution	Facilities of the National Center for Disease Control and Public Health (NCDC) inlcude main building located at 9, M. Asatiani str. Tbilisi, 0186, Georgia and Richard G. Lugar Center for Public Health Research (CPHR) located at 16, Kakheti highway. Tbilisi, 0109, Georgia The following spaces will be utlized for project impementation NCDC main building: Office #304, #305, #308 and #310. CPHR: #1150B, Richard G. Lugar Center Laboratory The following equipment is available for experimental and research activities:

	Biological Safety Cabinet, Class II, type 2A/B3; Thermocyclers, Techne - 3 units; Horizontal and vertical electrophoresis equipment, BioRad, Serva; PFGE BioRad CHEF-DR-II System; Blotting and Hybridization Equipment; Genetic Analysis System CEQ-8000 Beckman Coulter; Sequencer - ABI 3130XL; WGS - Illumina MiSeq platform; Ultracentrifuge; PCR Workstations; Water Baths; Autoclave; Thermostats.

II. Specific information

1. Introduction and Overview

Clostridium difficile is the major cause of pseudomembranous colitis and antibiotic-associated diarrhea. The typical manifestations of *C. difficile*-associated disease (CDAD) are abdominal cramps, profuse diarrhea (mucoid, greenish, foul-smelling and watery stools), low-grade fever and leukocytosis. *C. difficile* is estimated to colonize 3% of healthy adults, 66% of infants, and 15% to 25% of hospitalized patients. However, *C. difficile* rarely causes problems in children or healthy adults, as it is kept in control at low levels or is outcompeted by the normal bacterial population of the intestine. When certain antibiotics disturb the balance of bacteria in the gut, *C. difficile* can multiply rapidly and produce toxins which cause illness. The prevalence of CDAD is increasing worldwide due to broad-spectrum antimicrobial use. Transmission of *C. difficile* occurs mainly via contact of colonized health care workers to patients or directly by patient-to-patient transmission. Spores of *C. difficile* may survive in the environment for very long periods of time and also show resistance to various surface disinfection substances. By this, the route "patient – environment – patient" is possible for nosocomial *C. difficile* transmission. Risk factors healthcare-associated CDAD: antimicrobial use, advanced age (>65 years), laxative use, proton pump inhibitors, anti-neoplastic chemotherapeutic use, renal insufficiency, gastrointestinal surgery/procedures, environmental contamination, severity of underlying disease, nasogastric intubation, gastric acid suppressants, duration of hospital stay, duration of antibiotic course, multiple antibiotics, and prolonged hospital stay. The financial impact of CDAD on the healthcare system is substantial (3 billion EURO/year in European Union and 1.1 billion USD/year in the USA).

Toxin A (TcdA coded by *tcdA*) and toxin B (TcdB coded by *tcdB*) of *C. difficile* play significant roles in colonic injury. Detection of toxins A and B in feces of humans with diarrhea is considered diagnostic for CDAD[29]. Some *C. difficile* strains produce a third, unrelated toxin (binary toxin, CDT); the role of CDT in CDAD is unknown. It has been believed that toxigenic strains produce *tcdA* and *tcdB* and that nontoxigenic strains produce neither; however, the appearance of variant strains with deletions of the *tcdA* gene (A-B+) and patients infected with A-B+ strains have been reported. In recent years, a new toxin-hyperproducing *C. difficile* strain, characterized as North American pulsed-field gel electrophoresis type 1 and polymerase chain reaction (PCR) ribotype 027 (NAP1/027), has been recognized in Europe, the United States, and Canada as an important cause of hospital outbreaks.

The epidemiology of CDAD is not well known in Georgia because there is an unjustified inattention to CDAD in hospitals and an absence of diagnostic testing.

2. Expected Results and Their Application

- Obtaining incidence of *C. difficile*-associated disease among hospitalized patients in Georgia
- Possible of risk factors of healthcare-associated-CDAD transmission in Georgia will be identified
- Relationships between *C. difficile* toxins A and B and CDAD
- Molecular characteristics of *C. difficile* strains prevalent in Georgia will be defined
- Formulation of preventive measures against *C. difficile*-associated disease based on the epidemiology of *C. difficile*-associated disease in Georgia

3. Meeting ISTC Goals and Objectives

- Providing weapons scientists and engineers in the CIS, particularly those who possess knowledge and skills related to weapons of mass destruction, opportunities to redirect their talents to peaceful activities;
- Promoting integration of scientists of CIS states into the international scientific community;
- Supporting basic and applied research and technology development for peaceful purposes, notably in fields of environmental protection, energy production, nuclear safety;
- Contributing to the solution of national or international technical problems (other than those mentioned above);
- Reinforcing the transition to market-based economies responsive to civil needs.

4. Scope of Activities

Task 1

Task description and main milestones	Participating Institutions
Data collection for *C. difficile*-associated disease prevalence and risk-factors investigation Preparation and developing of questionnaires/data collection forms. Working on the protocols. Development of questionnaires/data collection forms for survey of patients who will be involved in the project study Working on the protocols – develop protocols based on international experience of USA and EU. The epidemiological and laboratory surveillance data will be analyzed using SPSS. Databases will be created and data entry will be performed.	National Center for Disease Control and Public Health, Tbilisi, Georgia

	Description of deliverables
1	Data collection forms developed and implemented –progress report
2	Protocols developed – test protocol
3	A contemporary, computer-based epidemiological database will be established - progress report

Task 2

Task description and main milestones	Participating Institutions
Detection, isolation and identification of *C. difficile* strains from clinical samples using bacteriological methods. Determination the antimicrobial susceptibility profile of *C. difficile* strains Culturing *C. difficile* strains from the clinical samples plating onto selective agar plate called CCFA (cycloserine cefoxitin fructose agar). Isolation and identification of *C. difficile* strains from the clinical samples using bacteriological methods (study of microbes' morphology, colonies morphology and growth characteristics, biochemical tests). *C. difficile* isolates will be tested against metronidazole, moxifloxacin, vancomycin and clindamycin using E-test strips. The interpretation of MIC results is based on the recommendations given by the guidelines of CLSI.	National Center for Disease Control and Public Health, Tbilisi, Georgia

	Description of deliverables
1	Isolation and characterization of *C. difficile* strains using bacteriological methods – progress report, final report
2	*C. difficile* isolates tested according to the CLSI protocols – progress report, annual report, final report

Task 3

Task description and main milestones	Participating Institutions
Study of relationships between *C. difficile* toxins A/B and CDAD Detection with an ELISA for *C. difficile* toxins A and B Variables associated *C. difficile* toxins A/B and CDAD	National Center for Disease Control and Public Health, Tbilisi, Georgia

	Description of deliverables
1	Production of *C. difficile* toxins A and B will be measured by ELISA - progress report, annual report, final report

Task 4

Task description and main milestones	Participating Institutions
Study molecular epidemiology of *C. difficile* Toxin typing: For detection of toxin A, region *tcdA* will be tested and for toxin B – region *tcdB*. Presence of binary toxin will be tested by detection of the binary toxin genes *ctdA* and *cdtB*. PCR ribotyping: PCR ribotyping will be performed at AGES, Austria and NCDC, Georgia. For primary molecular typing of the strains *C. difficile* isolated during the project classic agarose gel-based ribotyping will be applied. Primers 16S and 23S will be used. The same primers will be used in capillary gel electrophoresis-based PCR ribotyping labelled at the 5' end with fluorescent dye appropriate to CEQ-8000, Beckman Coulter. Web database: Capillary gel electrophoresis-based PCR ribotyping results for Georgian isolates of *C. difficile* will be entered in the web-based database http://webribo.ages.at	National Center for Disease Control and Public Health, Tbilisi, Georgia

	Description of deliverables
1	*C. difficile* strains isolated during the project will be studied on presence of binary toxin genes – progress report, annual report, final report
2	Gel based and capillary PCR ribotyping will be performed for all received strains – progress report, annual report, final report
3	Web database will be created for Georgian strains of *C. difficile* – progress report

5. Role of Foreign Collaborators/Partners

A partnership research program will be established between scientists at the NCDC and U.S. collaborators. Dr. Dale L. Morse has extensive experience in study of epidemiology of *Clostridium difficile*-associated disease. The role of the US collaborator will be to Work with Georgian counterpart to communicate progress to BTEP.

The US Department of Health and Human Services / Biotechnology Engagement Program (BTEP), as the ISTC partner, will provide funding to transform the collaboration between Georgia participating institution and the US collaborating institution into the ISTC Partnership Project.

In frames of the collaboration with Dr. Dale L. Morse, the main points of collaboration will be: joint discussion of project results; meetings at conferences and direct visits, providing comments on the project reports and technical assistance; preparation of cooperative reports for conferences and joint publications. Dr. Dale L. Morse will also monitor progress achieved regularly and provide marketing information on manufacturers, prices and quality of laboratory materials needed for studies and participate in the generation, gathering and analysis of scientific data.

6. Technical Approach and Methodology

Data collection for *C. difficile*-associated disease incidence and risk-factors investigation

For all patients with *C. difficile*-associated disease the data will be collected from medical records, after appropriate informed consent, on the following possible risk factors and characteristics: patient's age and sex, admission date, patient's location(s) during admission, dates of prior hospitalization, culture date(s), culture source(s), procedures, underlying conditions and diseases, colonization status (if known), and clinical signs and symptoms of CDAD, antimicrobial therapy and etc.

Specimen collection

Specimen will be submitted in a clean, watertight container. Samples collection will be conducted as soon as possible after onset of symptoms. In case tests cannot be performed rapidly specimens will be stored at 4^0C (for up to 24 hours of collection) or frozen at -20^0C if the stool will be unable to be processed within 24 hours of collection. Specimens will be transported to the laboratory and processed as soon as possible. If the initial stool sample testing will be negative for *C. difficile*, it may be useful to test additional diarrheal specimens from the same patient. Testing three stools can increase the likelihood of a positive test by 10%.

Bacteriological test

For culture isolation of *C. difficile,* stool specimens will be used generally used. For an optimal bacteriological diagnosis, only liquid stools should be accepted, except in the case of an epidemiological investigation. Due to a rapid loss of cytotoxin activity, only fresh specimens should be processed and they should be stored at 4^0C or less, in case tests cannot be performed rapidly. On the other hand, cultures of *C. difficile* remain unaffected by ambient storage due to sporulation. Repeated samples within 7 days of the initial request seem to give little useful information.

It is recommended to use a selective microbial medium, CCFA (cycloserine cefoxitin fructose agar) for the isolation of *C. difficile*. The selective agents are cycloserine at a concentration of 500 mg/L and cefoxitin at 16 mg/L. These concentrations were reduced to 250 and 8 mg/L, respectively, in some studies. The original formulation included egg-yolk, which may be replaced by blood. Stools will be directly inoculated and incubated in an anaerobic atmosphere for 48 h at 37^0C with anaerobic pre-incubation of the plate, which improves the recovery rate. Addition of pure sodium taurocholate or taurocholate at a concentration of 1 g/L allows for better spore germination and is suitable for environmental cultures or in cases of negative culture with positive fecal cytotoxin. The sodium salt of cholic acid is just as effective as pure taurocholate in stimulating spore germination. Pretreatment of stools with ethanol-shock (equal volumes of ethanol and feces mixed for 1 h before inoculation) has also been shown to increase the sensitivity of culture. Colonies of *C. difficile* are easily recognized on culture plates due to their typical morphology (ground glass appearance) when observed with binoculars. A yellow-green or chartreuse fluorescence under ultraviolet illumination is another characteristic of the colonies but this may vary with the medium used. Suspected colonies based on their morphology will be picked for further characteristic. By staining with the Gram stain *C. difficile* isolates are visible in light microscope as a Gram-positive spore-forming rod-shaped bacillus size from 0.5-1.9 μm wide, 3-16 μm long. Biochemical methods have not found wide application in clinical practice and research because of their low specificity, however, *C .difficile* is oxidase and catalase negative which will be performed during the study. Cytotoxin detection is often considered as the standard for the diagnosis of *C. difficile* infections. This method consists of inoculating a filtrate of a stool suspension into a cell culture and observing a cytopathic effect as a consequence of disruption of the cell cytoskeleton; which results in cell rounding in many cell lines. The effect is mainly due to toxin B, which is 1000 times more cytotoxic than toxin A.

Antimicrobial susceptibility testing

Isolates will be tested against metronidazole, moxifloxacin, vancomycin and clindamycin using epsilon test (E-test) strips. A suspension of *C. difficile* equivalent to 1 McFarland turbidity standard will be spread out on Brucella agar supplemented with hemin and vitamin K1 and incubated in anaerobic atmosphere at 37^0C. The MIC (minimal inhibitory concentration) will be read after 24h, excluding clindamycin (read after 48h), given through the intersection of the inhibition ellipse on the scale. The interpretation of MIC results will be based on the recommendations given by the guidelines of the Clinical and Laboratory Standards Institute (CLSI) for metronidazole, clindamycin and moxifloxacin. The breakpoints for metronidazole are ≤ 8 μg/ml for susceptible, 16 μg/ml for intermediate, and ≥ 32 μg/ml for resistant. The breakpoints for clindamycin are ≤ 2 μg/ml for susceptible, and ≥ 8 μg/ml for resistant. Moxifloxacin resistance is determined using a breakpoint of ≤ 2 μg/ml for susceptible and ≥ 8 μg/ml for resistant; high-level-Moxifloxacin resistance is determined using a breakpoint of ≥ 32 μg/ml. For vancomycin we will use breakpoints of ≤ 2 μg/ml for susceptible, 4 to 16 μg/ml for intermediate, and ≥ 32 μg/ml for resistant, as no standard is defined by CLSI.

Detection *C. difficile* toxins A and B

In-vitro production of toxins A and B will be measured by enzyme-linked immunosorbent assays (ELISA) in culture supernatants from a 1 mL subsample of the culture. We will measure toxin production at 24 h, 48 h, and 72 h. We will measure toxin A and B concentrations by capture ELISA with specific polyclonal antibodies. Briefly, microplates will be coated overnight with antitoxin A or antitoxin B goat IgG (2 μg/mL) in carbonate-

bicarbonate buffer (pH 9·8). Plates will be blocked with 2·5% skim-milk buffer in Dulbecco's phosphate-buffered saline and 0·05% Tween 20 (blocking buffer) at 37°C for 90 min. We will then prepare culture supernatants, standards and controls, using blocking buffer, and these will be incubated for 1 h at 37°C (100 µL/well). After washing, cultures will be incubated with antitoxin A or antitoxin B mouse-specific IgG for 1 h at 37°C and then detected by goat anti-mouse IgG coupled to alkaline phosphatase, with the use of diolamine as substrate.

Molecular epidemiology

Toxin typing

Toxins will be typed as described by van den Berg et al. (2004). For detection of toxin A, region *tcdA* will be tested using primers NKV011 (5'-TTTTGATCCTATAGAATCTAACTTAGTAAC-3') and NK9 (5'-CCACCAGCTGCAGCCATA-3'). For the detection of toxin B, region *tcdB* will be tested using primers NK104 (5'-GTGTAGCAATGAAAGTCCAAGTTTACGC-3') and NK105 (5'-CACTTAGCTCTTTGAT TGCTGCACCT-3') as described previously.

Presence of binary toxin will be tested by detection of the binary toxin genes *ctdA* and *cdtB* using primers and conditions as described by Stubbs et al. (2000): for *ctdA*, forward primer ctdAfw (5'-TGAACCT GGAAAAGGTGATG-3') and reverse primer ctdArev (5'-AGGATTATTTACTGGACCATTTG-3'); for *ctdB*, forward primer ctdBfw (5'-CTTAATGCAAGTAAATACTGAG-3') and reverse primer ctdBrev (5'-AACGGATCTCTTGCTTCAGTC-3').

PCR ribotyping

For primary molecular typing of the strains *C. difficile* isolated during the project classic agarose gel-based ribotyping will be applied. Primers 16S (5'-GTGCGGCTGGATCACCTCCT-3') and 23S (5'-CCCTGCACCCTTAATAAC TTGACC-3') will be used.

The same primers as listed above will be used in capillary gel electrophoresis-based PCR ribotyping labelled at the 5' end with fluorescent dye appropriate to CEQ-8000, Beckman Coulter.

Web database.

Capillary gel electrophoresis-based PCR ribotyping results for Georgian isolates of *C. difficile* will be entered in web-based database (http://webribo.ages.at).

Statistical analyses

The statistical analyses will be performed with SPSS software. The statistical tests that will be used includes particularly Pearson's correlation coefficient, cumulative incidence, and HA-CDAD incidence density and x^2 test for influence of selected risk factors on incidence and mortality and the distribution of risk factors of HA-CDAD in patients. A P value < 0.05 will be considered statistically significant.

To calculate HA-CDAD rates, epidemiological staff will collect monthly the number of patients in departments of study hospitals. The overall HA-CDAD patient and patient-day rates will be calculated by dividing the total number of HA-CDAD pooled throughout all months. Infection rates will be calculated for each group and for fairer comparisons between groups.

7. Technical Schedule

	Quarter 1	Quarter 2	Quarter 3	Quarter 4	Quarter 5	Quarter 6	Person*days
Task 1	Test protocol	Progress report	Progress report	Annual report	Progress report	Final report	
Person*days	**85**	**101**	**101**	**107**	**107**	**75**	**576**
Task 2	Progress report	Progress report	Progress report	Annual report	Progress report	Final report	
Person*days	**69**	**85**	**85**	**85**	**85**	**30**	**439**
Task 3	Progress report	Progress report	Progress report	Annual report	Progress report		
Person*days	**24**	**24**	**24**	**24**	**24**		**120**
Task 4	Test protocol	Progress report	Progress report	Annual report	Progress report	Final report	
Person*days	**64**	**64**	**64**	**68**	**68**	**68**	**396**
TOTAL	**242**	**274**	**274**	**284**	**284**	**173**	**1531**

8. Personnel Commitments

8.1. Individual participants

Leading Institution: NCDC

Category I (weapon scientific and technical personnel)

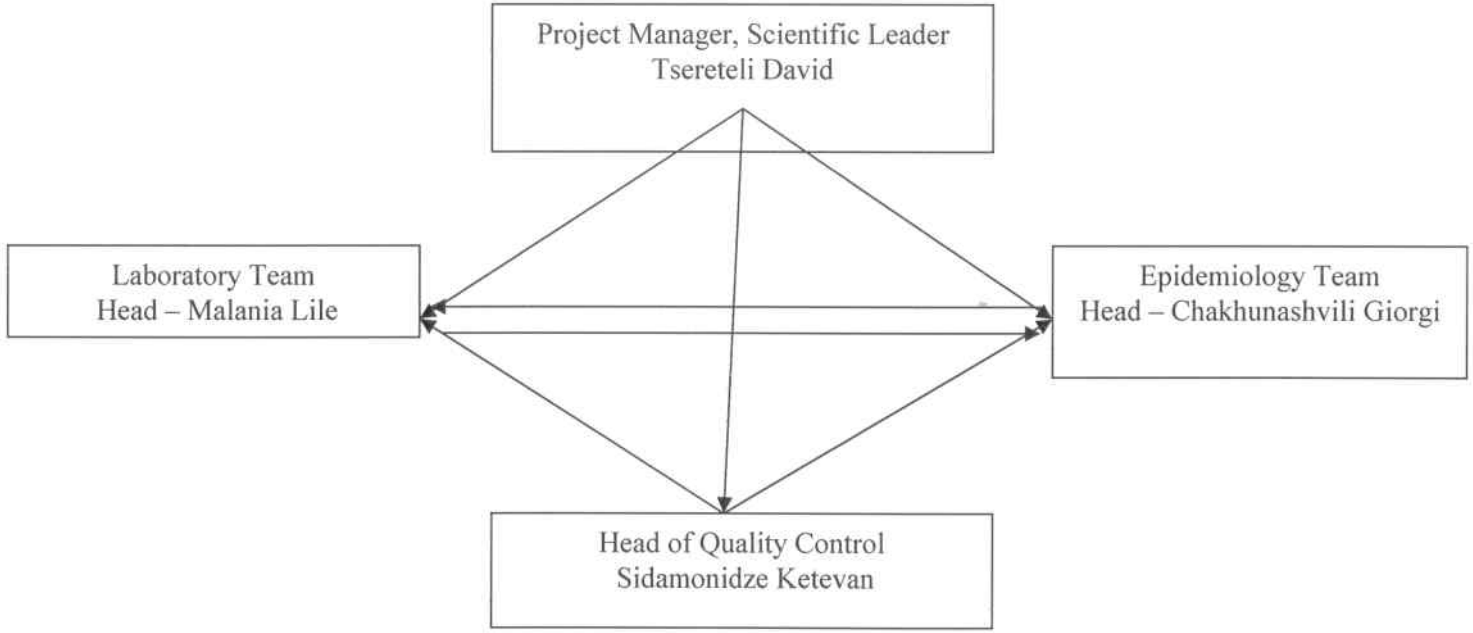
Name	Birth Year	Scientific Title	Weapon Expertise Ref.	Function in project	Daily rate (US$)	Total days	Total grants (US$)
Tsereteli David	1964	M.D., Ph.D.	3	Project Manager Scientific Leader	50	180	9000
Zangaladze Ekaterine	1956	M.D., Ph.D.	3	Mol. Biology research	45	96	4320
Kekelidze Merab	1955	Ph.D.	3	Mol. Biology research	45	80	3600
Malania Lile	1978	M.D., Ph.D.	3	Head of Laboratory Team	45	120	5400
Zhghenti Ekaterine	1975	B.A.	3	Mol. Biology research	40	120	4800
Zakhashvili Khatuna	1964	M.D.	3	Epidemiological research	40	90	3600
Shutkova Tatiana	1956	Ph.D.	3	Bacteriological research	40	64	2560
Tevzadze Liana	1941	M.D.	3	Bacteriological research	35	75	2625
Kiknadze Nino	1962	B.A.	3	Bacteriological research	35	100	3500
Chikviladze Tamar	1959	M.D.	3	Serological research	35	90	3150
					Total:	**1015**	**42555**

Category II (other scientific and technical personnel)

Name	Birth Year	Scientific Title	Function in project	Daily rate (US$)	Total days	Total grants (US$)
Sidamonidze Ketevan	1978	M.D.	Head of Quality Control	35	168	5880
Chakhunashvili Giorgi	1986	M.D., Ph.D.	Head of Epidemiology Team	35	144	5040
Sanadze Ketevan	1965	M.D.	Epidemiological research	30	102	3060
Chlikadze Rusudan	1963	M.D.	Epidemiological research	30	102	3060
				Total:	**516**	**17040**

8.2. Managerial responsibilities

Among the project 2 work-groups will be created: Epidemiology and Laboratory (Bacteriology, Serology and Mol. Biology). To implement the project effectively, Dr. Sidamonidze Ketevan will quality control the data collection and laboratory work as well as data entry and will report to the project manager on the weekly bases. The project manager will be responsible for the management of project activities over the project duration. Manager's responsibility will also include the monitoring of project budget.



9. Financial Information

TABLE 1

Estimated Aggregated Expenditures by Recipient

Category	Quarters 1 & 2		Year 1		Year 2		Total	
	(1)	(2)	(1)	(2)	(1)	(2)	(1)	(2)
1 Grant Payments:								
1.1 Category I		14590		30120		12435		42555
1.2 Category II		5400		11440		5600		17040
1.3 Category III								
1.4 Category IV								
Total Grant Payments		**19990**		**41560**		**18035**		**59595**
2 Equipment:								
2.1 Capital Equipment								
2.2 Non-Capital Equipment								
Total Equipment								
3 *Materials/Supplies*	**1000**	**21525**	**1000**	**21525**			**1000**	**21525**
4 Bank Fees	**20**	**400**	**35**	**620**	**15**	**180**	**50**	**800**
5 Other Direct Costs:								
5.1 Technological Energy								
5.2 Communications	110		220		110		330	
5.3 Subcontracts/Seminars								
5.4 Logistics/Customs	200	1600	200	1600			200	1600
5.5 Other								
Total ODC	**310**	**1600**	**420**	**1600**	**110**		**530**	**1600**
6 Travel:								
6.1 Internal ***								
6.2 Outside CIS		6850		6850		5050		11900
Total Travel		**6850**		**6850**		**5050**		**11900**
Overhead/Retainage	.....	.....	.....	.....	.....	.....	3000	.....
Subtotals	**1330**	**50365**	**1455**	**72155**	**125**	**23265**	**4580**	**95420**
Totals	**51695**		**73610**		**23390**		**100000**	

Remarks: * (1) - Cash flow through Recipient Account
** (2) - Cash flow through ISTC
*** Include Local and inside CIS travel

10. Equipment and Materials Summary

10.1. Equipment Summary - No

10.2. Materials Summary

TABLE 3

EQUIPMENT/MATERIAL SUMMARY

MATERIAL SUMMARY

for Project Agreement #G-1759

To be provided in kind [X]
To be purchased by recipient [ ]

The ISTC will normally provide the most appropriate equipment that will perform the functions required; however, if very special reasons are given and explained in detail (Form PR-2E), the purchase of a particular make will be considered.

Please list items in the order of their priority and put an 'X' in the column next to "Item no." if ISTC form PR-2E, "Data for a Single Equipment Item', has been completed for a given item and is attached.

Item No.		DESCRIPTION OF ITEM	Date needed (quarter)	Qty	Unit cost (USD)	Amount (USD)
Leading Institution: NCDC						
1		Inoculating Loop (1µL) 500 EA, Sigma cat. # I8263	1-2	3	220	660
2		ART Barrier Pipette tips 200; 200µL sterile; PK of 10 trays; Thermo Scientific;cat # 2069-HR	1-2	2	90	180
3		Microcentrifuge tube (sterile), 2mL, high-impact resistant, screw-cap with integral O-ring, USA Scientific, Pk of 200; cat # 1420-9600;	1-2	1	105	105
4		Universal sample container with spoon cap; plain label, 400 EA in PK, Sigma, cat.# Z645389,	1-2	1	250	250
5		Etest Metronidazole MZH 256, 30 strips, bioMérieux, #530010	1-2	1	250	250
6		Etest Moxifloxacin MX 32, 30 strips, bioMérieux, cat #529010	1-2	1	250	250
7		Etest Vancomycin VA 256, 30 strips, bioMérieux, cat #525510	1-2	1	250	250
8		Etest Clindamycin CM 256, 30 strips, bioMérieux, cat #509510	1-2	1	250	250
9		Gram Staining Kit, Fluka, cat.#77730	1-2	1	90	90
10		Simultaneous detection of *C. difficile* toxins A and B tbcBIOMICS, cat #TGC-E001-1 –USD X	1-2	2	600	1200
11		Separate detection of *C. difficile* toxins A and B tbcBIOMICS cat #TGC-E002-1	1-2	2	600	1200
12		Millex-GP syringe filter unit, disposable; pore size 0.22 µm, diam. 33 mm, sterile; γ-irradiated, pack of 50 EA, cat. # Z359904, Sigma	1-2	2	250	500
13		QIAamp DNA Mini Kit, 250; Qiagen, cat. #51306	1-2	1	1100	1100
14		QIAamp DNA Stool Mini Kit, 50; Qiagen, cat #51504	1-2	2	350	700
15		Taq PCR Master Mix Kit, 1000; Qiagen, cat # 201445	1-2	1	700	700
16		Microcentrifuge Tubes, 1.5mL; Sterile; 50 tubes/bag,	1-2	1	290	290

		10 bags/unit; 10 units/case. Thermo Scientific; cat # 3457				
17		Proteinase K, (2ML), Qiagen, cat #19131	1-2	2	100	200
18		Oligonucleotide primers (order for the synthesis of oligonucleotide primers will be given to the company Integrated DNA Technologies – IDT, USA)	1-2			4000
19		Best N-Dex Laboratory Grade Gloves, powder-free, size S, Cole-Parmer, cat # EW-86287-80	1-2	2	350	700
20		Best N-Dex Laboratory Grade Gloves, powder-free, size M, Cole-Parmer, cat # EW-86287-81	1-2	1	350	350
21		Aerosol Resistant Tips, ART 10 Reach, 10µl; Thermo Scientific; Case of 4800; cat#2140; (Pk)	1-2	5	150	750
22		Aerosol Resistant Tips, ART 20P ; Thermo Scientific; Pk; cat#2149P-HR.	1-2	4	150	600
23		Aerosol Resistant Tips, ART 100; Thermo Scientific; PK; cat# 2065-RI	1-2	4	150	600
24		Aerosol Resistant Tips, 5 to 300µL; Thermo Scientific, cat #94052-350	1-2	4	150	600
25		ART Barrier Pipette tips ;Thermo Scientific; 1000E; 1000µL sterile tip, cat # 5479E	1-2	4	150	600
26		Tube Strips with Individually Attached Bubble Caps Case of 10, Cole-Parmer, cat # 53509-304	1-2	1	1500	1500
27		HotStarTaq Master Mix Kit (1000 U), Qiagen, cat #203445	1-2	1	900	900
28		POP-4 Polymer 5000mkl, Applied Biosystems, cat #402838	1-2	1	1000	1000
29		Geneflo™ 625 Size Standard Fluorescent DNA Ladder,(100 load) TAMRA-Labeled; Applied Biosystems , cat #3126	1-2	2	90	180
30		Hi-Di™ Formamide, 25ml, Applied Biosystems, cat# 4311320	1-2	1	100	100
31		MicroAmp Optical 96well Reaction Plate, (10pk) Applied Biosystems, cat # 8010560	1-2	3	220	660
32		MicroAmp caps, 8 Caps/Strip, Applied Biosystems, cat # 8010535	1-2	3	200	600
33		310 Running Buffer, 10X, Applied Biosystems, cat #402839	1-2	2	105	210
					Subtotal:	**21525**
					Estimated TOTAL COST:	**21525**

Form PR-1M of 3/98

TABLE 3-1

EQUIPMENT/MATERIAL SUMMARY

MATERIAL SUMMARY

for Project Agreement # G-1759

To be provided in kind [ ]
To be purchased by recipient [X]

The ISTC will normally provide the most appropriate equipment that will perform the functions required; however, if very special reasons are given and explained in detail (Form PR-2E), the purchase of a particular make will be considered.

Please list items in the order of their priority and put an 'X' in the column next to "Item no." if ISTC form PR-2E, "Data for a Single Equipment Item', has been completed for a given item and is attached.

Item No.		DESCRIPTION OF ITEM	Date needed (quarter)	Qty	Unit cost (USD)	Amount (USD)
Leading Institution: NCDC						
1		CCFA (cycloserine cefoxitin fructose agar) plates	1-2	400	2.00	800
2		Brucella agar supplemented with hemin and vitamin K1	1-2	100	2.00	200
					Subtotal:	**1000**
					Estimated TOTAL COST:	**1000**

Form PR-1M of 3/98

10.4. Other Direct Costs Summary

TABLE 4

OTHER DIRECT COSTS SUMMARY

OTHER DIRECT COSTS SUMMARY

for Project Agreement # G-1759

To be provided in kind [X]
To be purchased by recipient [ ]

Detailed breakdown of Other Directs Costs to include planned activities under items 5.1, 5.2, 5.3, 5.4, 5.5 from Table 1 of the Project Agreement

Item No.		DESCRIPTION OF ITEM	Date needed (quarter)	Qty	Unit cost (USD)	Amount (USD)
Leading Institution: NCDC						
1	5.4	Logistics/Customs	1-2			1600
					Subtotal:	**1600**
					Estimated TOTAL COST:	**1600**

Form PR-1OD of 3/04

TABLE 4-1

OTHER DIRECT COSTS SUMMARY

OTHER DIRECT COSTS SUMMARY

for Project Agreement # G-1759

To be provided in kind [ ]
To be purchased by recipient [X]

Detailed breakdown of Other Directs Costs to include planned activities under items 5.1, 5.2, 5.3, 5.4, 5.5 from Table 1 of the Project Agreement

Item No.		DESCRIPTION OF ITEM	Date needed (quarter)	Qty	Unit cost (USD)	Amount (USD)
Leading Institution: NCDC						
2	5.2	Mobile Communications, Post service	1-6			330
4	5.4	Customs	1-2			200
					Subtotal:	**530**
					Estimated TOTAL COST:	**530**

ANNEX II
General Conditions

Contents:

Annex II General Conditions

Part A - Implementation of the Work
Article 1 - General Provisions

1.1 The Recipient shall make best efforts to achieve the objectives of the Project and shall comply with all laws of the Republic of Georgia applicable to the Project. If in the course of project implementation deliverables are identified that may qualify under export control restrictions, the Recipient takes responsibility for obtaining the corresponding export licenses, in a timely fashion and operating in compliance with all Russian, CIS and International laws and regulations.

1.2 The Recipient shall, in particular, comply with all applicable laws and regulations related to safety.

1.3 The Recipient shall notify the Center's Project representative and the Partner without delay of:
(a) any event or circumstance which may materially affect the Project, and
(b) any proposal for significant changes of key personnel during the Project.

Article 2 - Subcontracting

2.1 Subcontracting shall require the advance written approval of the Center, with the concurrence of the Partner. However, approval shall not normally be given for subcontracting in any State that is not a Party to the ISTC Agreement unless the Center determines in writing that such subcontracting is essential for the Project.

2.2 The Recipient shall impose on a subcontractor the same obligations as apply to itself with respect to any rights of the Center or the Partner concerning the Project.

2.3 The provisions of Article 2.1 of this Annex shall not apply to Sub-Agreements pursuant to Article 3 of the Agreement or to orders for materials, equipment, and services which are incidental to or intended to facilitate the execution of the Agreement and placed in the normal course of business in accordance with the internal procedures and rules of the Recipient.

Article 3 - Monitoring of the Work

3.1 The Center shall:
(a) Have access to portions of facilities where the Project is being carried out and to all equipment, documentation, information, data systems, materials, supplies, personnel and services which concern the Project for monitoring the progress of the Project as described in Annex I;

(b) Be provided with technical and cost information concerning the management and progress of the Project requested at any time; and

(c) Give the Recipient not less than 20 days advance notice of any intended on-site financial auditing or technical monitoring of the Project.

3.2 The Recipient has the right to protect those portions of facilities that are not related to the Project.

3.3 After completion or termination of the Project, the Recipient may utilize the facility or portion of the facility previously used for the Project for other work. However, all documentation and records including those associated with equipment, data systems, materials, supplies and services utilized for the Project must be maintained and available for review by the Center for up to two years following the Project's completion or termination.

3.4 The Recipient shall, if requested by the Center, participate and assist in meetings to review or evaluate the Project during the lifetime of the Project.

Article 4 - Reports

4.1 The Recipient shall submit the following reports, in a suitable quality to enable direct reproduction, to the Center and the Partner for approval:

(a) A final report, in English and Russian, covering all the work, the objectives, the results and the conclusions, including a suitable summary of all these aspects; and
(b) Reports, as mutually agreed, prepared in a suitable form for publication and satisfactory to the Partner and the Center.

4.2 The Recipient shall submit any additional reports or any other deliverables specified in the Agreement.

4.3 The Recipient should clearly identify any reports or portions of reports that contain invention or business confidential information as defined in Part E of this Annex. The final report shall include a statement that all inventions Made during the performance of work under the Agreement have been reported to the Center and to the Partner, or if no inventions were Made, a statement to that effect. The Recipient also may include a suitable disclaimer in any report against possible claims by third parties.

Article 5 - Completion or Expiration of the Agreement

5.1 The Agreement shall be deemed to be completed on the approval by the Center and the Partner of the last deliverable required or last payment by the Center, whichever shall be the later.

5.2 Subject and without prejudice to the provisions in Part D of this Annex, the Recipient shall be deemed to have discharged its obligations with respect to the performance of the work after the approval of all the reports and any other deliverables required by the Agreement.

Part B - Payments
Article 6 - Payments by the Center to the Recipient

Payments of allowable costs other than the Center's in-kind contributions, the Center's grant payments to Individual Participants and overhead payments shall be made in accordance with the following principles.

6.1 Cost statements shall be expressed in US dollars unless otherwise specified in the Agreement. All payments by the Center shall be made in that currency unless otherwise agreed.

6.2 The financial contribution by the Partner through the Center shall be paid in installments as specified in Article 5 of the Agreement.

6.3 If the Center or the Partner considers that the work has not effectively been commenced within three months of the payment of the first advance, the Center may require the reimbursement of the advance together with any interest earned on the advance. Any reimbursements will be returned to the Partner account.

6.4 If on completion, cessation, or termination of the work, the payments made by the Center exceed the actual allowable costs, the Recipient shall promptly reimburse the difference to the Center. Interest may be added to this amount at the prevailing market rate as determined by the Center one month after the reimbursement date specified by the Center. Any reimbursements will be returned to the Partner account.
6.5 Subject to Article 12 of this Annex, periodic payments made against cost statements shall be considered as advances until acceptance of the appropriate deliverables, in accordance with Annex I, or, if no deliverables are specified, until acceptance of the final report.

Part C - Allowable Costs
Article 7 - Accounting Principles, Allowable Costs, and Transfer of Costs

7.1 The original estimates of expenditures set forth in Annex I may be adjusted by the Recipient between categories without the prior approval of the Center, except for reductions in personnel costs and increases in travel costs, and provided that the transfers do not fundamentally affect the scope or content of the Project.

7.2 The Recipient shall ensure that no unnecessary cost or unnecessarily high or extravagant cost is charged to the Agreement.

Article 8 - Direct Costs

8.1 Personnel

8.1.1 Personnel costs shall be separated into four categories as described in Annex I and reflected in the reporting form in Annex III. Even though some or all of these costs may be reimbursed by the Center through direct grant payments to the Individual Participants, the Recipient is responsible for certifying the time devoted to the Project by the Individual Participants and for maintaining necessary documentation to support such certification.

8.1.2 Personnel costs shall be charged to reflect the actual eight-hour days, or one-half days when appropriate, worked by personnel assigned by the Recipient to the Project in accordance with Annex I. Work periods of less than four hours may not be charged.

8.1.3 Personnel costs for a specific period of time may not be charged to this Project if reimbursement (except regular employment salary) is being received from other sources for the same period of time.

8.1.4 The Project Manager may increase or decrease the time commitments of personnel by up to 10 percent during one year of any individual without approval of the Center, but may not change the daily rate without approval by the Center. The Project Manager may request more significant changes in the personnel commitments, including changes in the names of the personnel, at the beginning of each quarter with a brief explanation of the reasons for the changes. In unusual situations, the Project Manager may request changes during the quarter. The Center, in consultation with the Partner, will respond promptly to such requests. Changes in scientific personnel must provide for the new participants to have technical credentials and weapons experience comparable to those of the personnel they replace.

8.1.5 The Center will not reimburse personnel costs associated with holidays, annual vacations, overtime, or sick leave. Such additional costs, if any, are the responsibility of the Recipient.

8.1.6 The Project Manager shall ensure that the scheduling of annual leave by the Individual Participants does not interfere with accomplishment of the Work Plan in Annex I.

8.1.7 The Recipient is responsible for any medical expenses or compensation claims for injuries or other losses for personnel working on the Project which are directly or indirectly related to the Project.

8.1.8 Individual daily records of time devoted to the Project must be signed by all personnel assigned to the Project, and all records must be certified at least monthly by the Project Manager and for the Project Manager by another appropriate senior employee of the Recipient.

8.2 Equipment

8.2.1 Equipment shall be categorized as indicated in the reporting form in Annex III.

8.2.2 The cost of equipment used in the Project which is purchased, fabricated, or leased after the Operative Commencement Date may be charged as a direct cost. The total leasing cost of any piece of equipment shall not exceed the cost which would have been allowable for its purchase.

8.2.3 Notwithstanding Article 4.5.1 of the Agreement, the Center will retain the title to all the equipment provided to or procured by the Recipient using Center funds regardless of the acquisition per item cost of the equipment. The final decision of possible transfer of the title shall be taken by the Center, in consultation with the Finanacing Party by the time of completion, termination or cessation of the Project taking into account the specific legal, institutional and other factors in effect in the state of the Recipient at that time.

8.3 Materials

The costs of required materials shall be allowable costs. They shall be categorized as raw materials, laboratory supplies, safety devices and protective gear and other as indicated on the reporting form in Annex III.

8.4 Other Direct Costs

8.4.1 Other direct costs shall be categorized as indicated in the reporting form in Annex III.

8.4.2 Costs incurred by the Recipient in using its internal resources for performance of the Agreement such as costs associated with (a) testing facilities, (b) computer services, (c) special test equipment, (d) dedicated security services, and (e) dedicated accounting services, but excluding items covered by Article 9 of Annex II, may be charged as direct costs through valid cost allocation formulas approved by the Center to the extent such costs contribute to the Project, provided such facilities and services are open to access for monitoring and auditing in accordance with Article 9 of the Agreement. If costs incurred by the Recipient are not charged as direct costs, they may be presented as in-kind contributions of the Recipient.

8.5 Travel and Per Diem for the Recipient

Travel and per diem within the CIS shall be charged in accordance with the internal rules of the Recipient which are subject to approval by the Center. International travel shall be provided by the Center in accordance with Article 4 of the Agreement.

8.6 Sub-Agreements and Subcontracts

8.6.1 Subject to Article 2 of this Annex, costs of subcontracts shall be allowable costs and shall be included as discrete entries in the appropriate categories on the reporting form of Annex III. If the subcontractor is a scientific institution engaged in a sub-agreement pursuant to Article 3 of the Agreement, costs are allowable only to the extent that they would be allowable if incurred directly under the Agreement. In selecting a subcontractor other than a scientific institution pursuant to Article 3 of the Agreement, the Recipient shall compare prices and quality of several subcontractors and choose the most cost-effective offer. For any subcontract costing more than the equivalent of $25,000, the Recipient shall organize a bidding process. For any subcontract costing between $10,000 and $25,000 (equivalent) written quotations shall be obtained from three sources to the extent possible.

8.6.2 Should the Recipient enter into a sub-agreement with a scientific institution pursuant to Article 3 of the Agreement, the reporting form in Annex III shall include the costs incurred pursuant to the sub-agreement which shall be supported by detailed information.

Article 9 - Overhead

A fixed payment may be charged with respect to overhead which covers items such as general administration, institutional management, depreciation of buildings and general equipment, maintenance of building and grounds, telephones, heating, lighting, electricity for the buildings and general staff training.

The payment shall not exceed 10% of the direct Project costs, excluding equipment, travel and subsistence.

Since the overhead will be retained by the Center until acceptance of the final report, the Recipient need not include this item on the reporting form in Annex III.

Article 10 - Costs Not Allowed

Allowable costs shall not include, among others:

- any profit;
- any contributions to pension, medical, or other social funds;
- any provisions for possible future losses or liabilities;
- any taxes, including profit tax, value added tax, personal income tax, and local taxes, as well as any other tariffs, dues, custom duties, import duties, fees, or other imposed taxes or similar charges;
- any costs allocatable to other projects.

The Center will determine the use of any interest earned from funds provided by the Center or return on investment of such funds. Such interest or return on investment must be reported to the Center.

Part D - Justification of Costs and Auditing
Article 11 - Books of Account and Documentation

The Recipient shall maintain, in accordance with the accounting practices set forth in the Agreement, proper books of account and appropriate documentation, such as invoices and time sheets to support and justify the costs reported. These shall be made available for audits by the Center during the period of the Project and for a period of up to two years following the Project's completion or termination.

Article 12 - Auditing

12.1 Cost statements are subject to verification even after the Center has reimbursed costs. The Center has the right pursuant to the ISTC Agreement and ISTC Statute to carry out on-site auditing of all activities of the Project. The Recipient will be given not less than 20 days notice of any intended audit. For the purposes of the audit, the Recipient shall make accessible all portions of facilities, equipment, documentation, information, data systems, materials, supplies, personnel and services related to the Project.

12.2 The Recipient has the right to protect those portions of facilities that are not related to the Project.

12.3 The Recipient shall maintain all documentation and records including those associated with equipment, data systems, materials, supplies and services utilized for the Project and shall make such documents, records and, to the extent possible, personnel available for auditing for a period of up to two years following the Project's completion or termination.

12.4 The Center shall have the right to select Courts of Auditors or other organizations or individuals to carry out audits of the Project; they shall be entitled to the same rights, should they choose to exercise them, as the Center with respect to access to, and verification of, any document under the Agreement for the purpose of any audit.

Part E - Information and Intellectual Property
Article 13 – Definitions

13.1 "Intellectual Property" includes inventions, patents, copyrights and other forms of protection provided by statutes, such as, industrial designs, design patents, mask works, and trademarks, and has the meaning defined in Article 2 of the Convention Establishing the World Intellectual Property Organization, done in Stockholm on July 14, 1967, which states: "Intellectual Property shall include the rights relating to:

- literary, artistic and scientific works,
- performances of performing artists, phonograms, and broadcasts,
- inventions in all fields of human endeavor,
- scientific discoveries,
- industrial designs,
- trademarks, service marks, and commercial names and designations,

- protection against unfair competition,
- and all other rights resulting from intellectual activity in the industrial, scientific, literary or artistic fields."

13.2 "Information" includes technical data and computer software and means recorded data of any kind of a scientific or technical nature, regardless of the form or method of recording, and capable of being read by a human being or processed by a machine.

13.3 "Foreground Results" means Foreground Information and Foreground Intellectual Property.

13.4 "Foreground Information" means Information, including all kinds of results, generated in the execution of this Agreement.

13.5 "Foreground Intellectual Property" means rights in Intellectual Property generated in the execution of this Agreement by the Recipient or any person employed or engaged by the Recipient.

13.6 "Background Results" means Background Information and Background Intellectual Property.

13.7 "Background Information" means Information, excluding Foreground Information, owned or controlled by either the Recipient or Partner in the same or related fields as the research under this Agreement and generated outside this Agreement.

13.8 "Background Intellectual Property" means rights in Intellectual Property, excluding Foreground Intellectual Property, owned or controlled by either the Recipient or Partner in the same or related fields as the research executed under this Agreement and originating outside this Agreement.

13.9 "Business Confidential Information" is also known as trade secret information and means technical, commercial or financial information, which:

Has been held in confidence by its owner;
Is not generally known or available from other sources;
Has not been made available by its owner to other parties without an obligation concerning its confidentiality;
Has not been independently developed by the receiving party; and
Is not available to the receiving party without obligations concerning confidentiality.

13.10 "Invention Information" is Intellectual Property which is to be protected by a patent and on which a patent has not been filed.

13.11 "Made," when used in relation to any invention, means the conception or first actual reduction to practice of such invention.

13.12 "Unlimited rights" means the right to use, modify, reproduce, perform, display, release, or disclose Information in whole or in part, in any manner, and for any purpose whatsoever, and to have or authorize others to do so.

Article 14 - Promotion of Technology and Project Results

Confidentiality

14.1 Subject to Article 4.1(c), all reports or portions of reports properly marked as Invention Information or Business Confidential Information by the Recipient in consultation with the Partner shall be protected from public dissemination unless otherwise agreed by the Recipient and the Partner. Invention Information is treated as Business Confidential Information until a patent application has been obtained unless such information so disclosed is or becomes legitimately available to the receiving Signatory Party through other means or sources

without any covenant as regards its confidentiality. Nevertheless, Business Confidential Information may be disclosed if the disclosure is required by law, regulation, or court order.

14.2 Subject to any obligations under this Agreement and in accordance with applicable laws and regulations, the Signatory Parties agree to keep confidential any Invention Information or Business Confidential Information communicated to them by other Signatory Parties or third parties in relation to the execution of this Agreement, unless such information so disclosed is or becomes legitimately available to the receiving Signatory Party through other means or sources without any covenant as regards its confidentiality. Nevertheless, Business Confidential Information may be disclosed if the disclosure is required by law, regulation, or court order.

Technology Promotion

14.3 The ISTC shall be entitled to publish general information on this Agreement including the identities of the Recipient and Partner, the title and objective of the Agreement, its estimated costs and duration, and the names of managers and laboratories where the research is being carried out.

14.4 Each Signatory Party agrees to submit to each other Signatory Party for review and approval a copy of any proposed publication of Foreground Information at least thirty days before such publication.

14.5 Any public communication or publication concerning this Project will acknowledge the Recipient, the Partner and the cooperative support of the ISTC.

14.6 Subject to the restrictions of Article 14.1, each Party to the ISTC Agreement (hereinafter referred to as the "**ISTC Party**") and the ISTC have a non-exclusive, irrevocable, royalty-free license with the right to sub-license in all countries to translate, reproduce and publicly distribute scientific and technical journal articles, reports, and books directly arising under this Agreement. All publicly distributed copies of a copyrighted work arising from cooperation under this Agreement shall indicate the names of the authors of the work, unless an author explicitly declines to be named.

Article 15 – Ownership of Intellectual Property and Foreground Information

15.1 In accordance with the ISTC Statute, except for inventions created by United States Government employees, all rights worldwide to Intellectual Property arising under this Agreement, including patent protection for industrial property, belong to the Recipient (or its designee), which has the responsibility for providing adequate protection of such Intellectual Property. The Recipient and the Partner have agreed to protect and allocate such Intellectual Property among each other as specified in Article 16 below. Rights to inventions made by United States Government employees or made in Partner's laboratory shall be determined by the United States.

15.2 All rights worldwide to Foreground Information arising under this Agreement belong to the Recipient (or its designee). The United States Government, as represented by Partner, is granted a non-exclusive, irrevocable, royalty-free, worldwide license of unlimited rights in Foreground Information.

Article 16 - Protection and Exploitation

16.1 Intellectual Property Rights (IPR) Allocation

(i) The work conducted under this project is expected to generate new intellectual property by the Recipient and the Partner:

(ii) The protection and allocation of intellectual property created or furnished in the course of the cooperative research activities pursuant to this Agreement shall be provided in accordance with the Articles 16.2, 16.3, 16.4, 16.5, 16.6, 16.7, 16.8, 16.9 of the Annex II.

(iii) Any publications or presentations of information developed by the project participants shall acknowledge their funding support and shall be cleared by the institutions involved according with the existing procedures. Joint work is expected to result in joint authorship of publications.

(iv) The development of any new commercial products and commercialization of results are not expected to be the issue during the term of the project

(v) However if this proves otherwise, the Recipient and its Partner agree to notify one another as well as other Parties of the Agreement in a timely fashion of any invention or copyrighted works arising under this Project and to seek protection for such intellectual property in a timely fashion.

(vi) The Recipient and the Partner shall be responsible for the maintenance, protection and preservation of all intellectual property during the term of the project

16.2 Ownership and Non-exclusive License: With the exception of inventions made by employees of the United States Government, the Recipient owns worldwide rights to Intellectual Property arising under this Agreement. The United States Government as represented by the Partner shall determine the rights in inventions made by United States Government employees or made in U.S. Government facilities. The United States Government, as represented by partner, is granted in all Intellectual Property arising under this Agreement a non-exclusive, irrevocable, royalty-free, worldwide (except for the territory of the United States) license to practice or have practiced for or on behalf of the United States. Upon the request of the Partner (or its designee), the Recipient entity (or its designee) shall enter into negotiation with United States commercial entities for licenses for commercial purposes on fair and reasonable terms in territories other than the United States in all Intellectual Property arising under this Agreement.

16.3 Commercialization in the United States: Upon request by Partner, the Recipient shall assign to the Government of the United States as represented by Partner, subject to a royalty-free, irrevocable non-exclusive license to the recipient, the entire right, title, and interest in any Intellectual Property in the United States, including inventions, patents on inventions, and copyrights arising under the Agreement. The Government of the United States will obtain and pay for all costs of obtaining patent protection in the United States on those inventions that the Recipient and Partner mutually agree to obtain patent protection in the United States (See Article 16.6). All uses of the Intellectual Property by or for the Government of the United States are royalty free. When the Government of the United States as represented by Partner or Partner's designee, negotiates and executes a license for commercial purposes to use Intellectual Property within the territory of the United States, which are purposes other than those by or for the Government, compensation will be sought for all uses of the Intellectual Property.

16.4 Compensation for inventors: In accordance with the policies of the Partner, which provide that the inventive entity shall receive at least 15% of royalties received, the inventors will receive a portion of the royalty income. The remaining royalties will be applied to cover or offset expenses incurred in obtaining and maintaining patent protection; and any remaining royalty income, after paying patent expenses, will be shared equally between the Recipient and Partner. However, the inventor, or inventors as a group, will always receive at least 15% of the total royalties received each year in accordance with the policies of the Partner.

16.5 Disclosure of inventions within two months: A written disclosure of invention will be provided by the Recipient (or its designee) to the Partner within two months of the date on which the invention is Made. See Article 17.2

16.6 Election to file patent applications within six months: The Recipient will notify Partner within six months of reporting an invention of each territory, except for the territory of the United States, in which the Recipient elects to protect the invention through patenting. In the territory of the United States, election to file will be by mutual agreement of the Recipient and Partner, and if the parties are unable to agree within eight months of reporting an invention and the Partner has not requested assignment under 16.3, either the Recipient or Partner may elect, by notifying the other party, to obtain patent protection in the United States and the party electing to file will pay all patent costs and will not share royalties with the Party not electing to file. If the Recipient files for a patent in the United States, the Government of the United States, as represented by Partner, shall have a non-exclusive, irrevocable, royalty-free license to practice or have practiced for or on behalf of the United States. See Articles 16.3 for patent costs and 17.3.

16.7 Filing of patent applications: The Recipient will file the first patent application within twelve months of reporting the invention. Partner has right to file patent applications in the countries in which the Recipient does not elect to file. If the Recipient does not elect to file within eight months of the date on which the invention is Made, the Partner may file applications in all countries in which the Recipient does not elect to file, and the Recipient

will assign title to the invention to the Partner in those countries in which the Partner has filed. The Recipient will retain a non-exclusive irrevocable, royalty free license in the territory where the Partner has filed. See Article 17.3

16.8 Exploitation of Results: The Technology Implementation Plan required by Article 8.2 of the Project Agreement shall contain a listing of all inventions Made under the Agreement, the status of pending patent applications, or patent numbers, licenses granted and in negotiation, and relate the commercial results of the research performed under the Agreement with the anticipated commercial results and intellectual property rights described in the proposal submitted for the Agreement.

16.9 The Recipient will grant to the United States Government, as represented by Partner, under reasonable terms and conditions the right to use by or for the Government Background Results owned by the Recipient which are necessary for the Partner to exploit Foreground Results, provided that the Recipient is free to disclose such Background Results, that no major business interests of the Recipient oppose the granting of such right, that in making this opposition such interests are not abusively restricting the exploitation of such right and that granting such right is not restricted by the law or obligations to a third party. The Recipient will notify the Partner, with factual statements in the next monthly technical report, of all situations where: the Recipient is not free to disclose such Background Results; or a major business interest opposes the granting of such right to such Background Results; or the disclosure of such Background Results is restricted by law or obligations to a third party.

Article 17 - Reporting of Inventions

17.1 The Recipient will disclose to the Partner and the ISTC in an ISTC-approved form every invention Made under this Agreement within two (2) months of the date on which such invention is Made. These disclosures must be in sufficiently complete technical detail to convey a clear understanding, to the extent known at the time of the disclosure, of the nature, purpose and operation of the invention.

17.2 The Recipient and the Partner will notify the ISTC of each territory in which each (or their designees) decides to protect inventions through patenting within six (6) months of the reporting of such inventions in accordance with Article 17.1 above.

17.3 The Recipient and the Partner will file patent applications in each territory in which each (or its designee) decides in accordance with Article 17.2 above to protect each invention through patenting. The first patent application will be filed in the territory where the invention was Made within twelve (12) months of reporting the invention in accordance with Article 17.1 above. The remaining patent applications will be filed in the other territories within respective time periods to ensure that the priority date of the first patent application is obtained for these later filed applications. The Recipient and the Partner will provide each other and the ISTC with copies of all patent applications each (or its designee) files.

Article 18 - Background Results

The Recipient and the Partner have identified and agreed that the following Background Results may be used in the performance of work under this Agreement and may be needed to practice any Foreground Results of this Agreement:
Recipient's Background Results: *none.*
Partner's Background Results: *none*.

Recipient and Partner represent that the above-identified Background Results are available for licensing as of the effective date of this Agreement.

Article 19 - Conflicting Agreements, Laws and Regulations

19.1 Recipient certifies that it has not and will not enter into any agreement with a third party that grants to the third party rights to Foreground Results that may affect the exploitation or commercialization of Foreground Results received by the Partner under this Agreement.

19.2 Recipient shall notify the Partner and the ISTC of any restrictions by government laws or regulations which may materially and adversely affect the rights necessary for the performance of the work or the exploitation and commercialization of Foreground Results.

ANNEX III
Formats for Progress and Cost Reports

1. Format for Technical Reports

Quarterly reports shall specify the progress, any actual or proposed deviations and modifications to the Work Plan in Annex I, and the results obtained. The reports shall contain sufficient information to enable assessment of the progress and cooperation within the Project. The details of the Annual Report shall be agreed upon at an appropriate time by the Recipient and the Center's Project representative. A suggested format for quarterly reports is as follows:

I. Summary of Technical Progress (By task in the Work Plan)
II. Milestones Completed
III. Summary of Personnel Commitments
IV. Major Equipment Acquired
V. Description of Significant Travel
VI. Current Technical Status (on schedule, behind schedule, ahead of schedule)
VII. Delays, Problems, Suggestions
VIII. IPR Annex

The quarterly report should be between three and five pages (single space).

2. Financial Forms

(The templates for reports are to be provided separately by the Center.)

3. Submission Dates for Technical and Financial Reports:

Technical and Financial reports are due two weeks after the end of each fiscal year quarter:

March 15
June 15
September 15
December 15

Additional time (two weeks) shall be granted for reconciliation (adjustments) of end-of-year balances.

ANNEX IV
DISCLAIMER

It is understood and agreed to by the Recipient of this ISTC project that:

The project funding commitment of the ISTC is subject to and limited by the funds which are actually available by the ISTC Financing Party(ies) for this project;

The funding for each project comes from ISTC Financing Parties and/or Partners who might make their ISTC financial contribution in whichever currency considered appropriate;

As a matter of practice, the ISTC at present signs all project agreements in a single currency, the US dollar;

The project support given to this project by the ISTC Financing Party(ies) and/or Partners of the ISTC may be affected by causes, including currency fluctuation, which may require adjustments in the project budget.