

**PARTNER PROJECT AGREEMENT P509
(LBNL-T2-225 GE)**

between

DOE's Initiative for Proliferation Prevention Program

the Science and Technology Center in Ukraine,

and

**S. Durmishidze Institute of Biochemistry and
Biotechnology of NLE Agrarian University of Georgia
L. Sakvarelidze National Center for Disease Control and
Public Health**

Kyiv

Operative Commencement Date: _____

The Science and Technology Center in Ukraine (STCU) (hereinafter referred to as "**the Center**"),
the U.S. Department of Energy (DOE) Initiatives for Proliferation Prevention (IPP) Program (hereinafter referred to as "**the Partner**"), and
the leading Institution S. Durnishidze Institute of Biochemistry and Biotechnology of NLE Agrarian University of Georgia,
the L. Sakvarelidze National Center for Disease Control and Public Health,

(hereinafter referred together as "**the Recipient(s)**")
represented for the purpose of the signature of this Partner Project Agreement (hereinafter referred to as "**the Agreement**") by their authorized representatives, (with the Center, the Partner, and the Recipient(s) hereinafter referred to collectively as "**the Signatory Parties**"),

TAKING INTO ACCOUNT THE FOLLOWING CONSIDERATIONS:

The United States of America, Canada, Sweden and Ukraine signed the agreement establishing the Science and Technology Center in Ukraine on October 25, 1993 (referred to as "**the STCU Agreement**"),

The European Union has acceded to the STCU Agreement on November 26, 1998, and in so doing, replaced Sweden as a Party to the Agreement,

Additional States may accede to the STCU Agreement to participate in the activities of the Center. Georgia acceded to the STCU Agreement on March 18, 1998; Uzbekistan acceded to the STCU Agreement on December 29, 1997, Azerbaijan acceded to the STCU Agreement on June 27, 2003, Moldova acceded to the STCU Agreement on December 7, 2004,

The Center is a legal entity and has been accredited by the Ministry of Foreign Affairs of Ukraine as an intergovernmental organization with its headquarters in Kiev,

The Partner, established under the law of the United States of America is a legal entity that has been approved by the Center's Governing Board to participate in Center activities,

The Recipient(s) is a legal entity within Georgia, ,

The Governing Board of the Center approves a project to be funded by the Partner through the Center in the domain covered by the Agreement,

The Partner has agreed to provide financial support for such project,

As set forth in the STCU 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,

HAVE AGREED AS FOLLOWS:

Article 1 - Scope of the Agreement

The Recipient(s) shall carry out the work plan set forth in Annex 1 according to the conditions of the Agreement, subject to the provisions of the STCU Agreement, and the Statute of the Center (hereinafter referred to as "**the STCU Statute**") which govern in case of conflict. The activities carried out under the Agreement are entitled isolation and characterization of probiotics that selectively grow on milk oligosaccharides (hereinafter referred to as "**the Project**"). The scopes of work and relevant budget lines for each recipient entity are identified in the Annex 1. All Project Activities subject to this Agreement are to be executed by the Recipient(s), using only funding provided by the Center and/or sources approved by the Center. The Recipient Entity(ies) shall notify the Center immediately if it and/or other participating institutions determine at any time to utilize any other funding sources to execute such Project activities.

Article 2 - Duration of the Project

The duration of the Agreement shall be from the date of entry into force of the Agreement (hereinafter referred to as "**the Operative Commencement Date**") until completion of the Agreement. Subject to the applicable requirements in Article 6 "Audit and Monitoring of the Agreement", Article 7, "Ownership and Exploitation of Results from the Agreement," and Annex III herein, the Agreement shall be deemed to have been completed upon approval by Partner of all deliverables required by the Agreement and final payment to Recipient or termination of the Agreement pursuant to Article 11 herein, whichever is earlier. The duration of the Agreement is estimated to be 24 months.

Article 3 - Financial Contribution of the Partner through the Center

3.1 The total cost of the Project to the Center shall not exceed 260000\$. This total includes the cost of items described in Articles 3.2, 3.3, and 3.4 below.

3.2 The Center shall pay for items ordered by the Recipient, represented by the project manager: equipment, materials, subcontracts, other direct costs, and travel. The amount of such payments is estimated to be 91090\$.

3.3 The Center shall make grant payments directly to individual participants in the Project. The amount of such payments is estimated to be 161830\$. This total amount may be increased with the concurrence of the Partner and Center provided that such increase results from additional time worked on the project, rather than an increase in the rate of pay, and an offsetting reduction is made to the cost of items in article 3.2.

3.4 The Center will pay overhead to the Recipient(s), represented by its Director(s), in the amount of 2.8% of the direct project costs.

3.5 The Center will receive a fee for its service in the amount of 0% of the total project costs. This amount should be calculated in addition to the total cost of the project.

3.6 The Partner will deposit to Center's account funding for first year of the project in accordance with Article 7 of Annex 2. Project funds will be sent annually contingent upon a positive review of the project progress by the Partner. The entire amount of Partner's commitment is equal to 260000\$ that is the total cost of the project plus STCU's fee in accordance with Articles 3.1 and 3.5.

3.7 Within Ukraine, all cash payments will be made in the national currency of Ukraine. Conversion of US dollars to the national currency of Ukraine will be according to the exchange rate of the Interbank Rate of Ukraine. Within Georgia, Uzbekistan, Azerbaijan, and Moldova all cash payments will be made in U.S. Dollars or Euros where possible.

3.8 Title to the property purchased for performance of this Agreement in accordance with Article 3.2 shall be determined in Annex 1 by applying one of the following clauses:

3.8.1 title will vest in the participation institution at the time of delivery or

3.8.2 title will remain with the Center until termination or completion of the project, at which time title will be vested in accordance with Article 8 - Special Conditions or following to additional agreement between the STCU, Partner and Recipient(s) replacing Special Conditions.

3.9 Title to any goods (deliverables) purchased by Partner under this Agreement shall pass directly from Recipient to Partner at the time of delivery, subject to Partner's right of rejection upon inspection.

Article 4 - Cost Statements, Reports, and other Project Outputs

Quarterly cost statements shall be submitted by the Recipient to the Center. The quarterly cost statements will include a representation that all projects activities conducted by the Recipient during the preceding quarter were funded only with funding provided by the Center and that no other source of funding was utilized in carrying out such activities.

Quarterly progress reports shall be submitted by the Recipient to the Center, to the Partner and/or to the Technical Monitor as designated by the Partner and identified in Annex I - Work Plan (in English and Ukrainian (optional) or Russian (optional, if the project is located only in other CIS states)), in hard copy and in electronic format in accordance with Annex 3 - Reports. The format of the cost statements and quarterly progress reports will be provided by the Center.

Technical reports and other deliverables that are requested by the Partner shall be submitted by the Recipient to the Partner and/or Technical Monitor in accordance with Annex I and Annex III.

Article 5 - Confidentiality

5.1 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(s) and the Partner.

5.2 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 sources without any covenant as regards its confidentiality.

Article 6 - Auditing and Monitoring

6.1 Access by the Center and the Partner, through the Center, to the project site to carry out on-site monitoring and for the evaluation and the verification of the progress of the Project activities, and to do audits of costs shall be granted by the Recipient(s) including access to (a) 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, and (b) technical and cost information concerning the management and progress of the Project.

6.2 The Center will give the Recipient(s) up to 10 days advance notice of any intended on-site monitoring of the project.

6.3 The Recipient(s) has the right to protect those portions of facilities that are not related to the Project.

6.4 All documentation and records, including those associated with equipment, data systems, materials, supplies, and services utilized on the project must be maintained and made available for review by the Center, the Partner, or their representatives, for up to two years following the project's completion or termination.

Article 7 - Ownership and Exploitation of Results

7.1 The allocation of intellectual property arising from this Agreement and the responsibilities for protecting and exploiting such intellectual property should be established between the Recipient(s), the Partner and/or Technical Monitor, on behalf of the Partner, in the form of Annex 4.

7.2 Exploitation of results shall be limited to applications for peaceful purposes. In this regard, the Recipient(s) 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 Georgia, and international agreements and conventions to which Georgia, is a party.

Article 8 - Special Conditions

8.1 The special conditions specified in this Article shall prevail over other conditions specified in the Agreement.

8.2 Partner, upon agreement with Center and Recipient(s), may at any time, by written notice, make changes within the scope of this Agreement. If any such change causes an increase or decrease in the cost of, or the time required for, performance of any part of the work under this Agreement, whether or not changed by the order, or otherwise affects any other terms and conditions of this Agreement, Partner shall make an equitable adjustment in the Project Price, the delivery schedule, or both, and shall modify the Agreement.

Article 9 - Liability

9.1 The Signatory Parties accept the project team for the execution of the project and accept the project manager as the leader of the project team. The project manager shall be responsible for scientific, technical, personnel and financial activities related to the project, and shall have exclusive rights to handle all goods and services related to the project during its term. The director(s) of the institution(s) is liable for provision of general administrative and legal support to the project manager in connection with the execution of the Agreement.

9.2 The Center shall not be liable for nonperformance by the Partner or the Recipient(s) of their obligations under the Agreement.

9.3 The Center and Partner 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.

Article 10 - Disputes

Disputes arising during performance of the Agreement including, in particular, (1) a claim by the Recipient(s) for any payments deemed due; (2) an interpretation of a provision of the Agreement; or (3) a request for relief or approval related to the Agreement, shall be subject to the following procedure.

The Recipient(s) 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. 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(s) 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(s) shall, nevertheless, proceed diligently with the performance of the Agreement.

Article 11 - Suspension and Termination of the Agreement

11.1 Each Signatory Party shall reserve the right to suspend the Project or its part by issuing to the other Signatory Parties a notification of suspension which specifies the problem, the effective date, and the period of the suspension.

11.2 When the Project is suspended by the Center, and the period of the suspension expires and the Center and the Recipient are unable to find a solution, the Center shall, in consultation with the Partner, terminate the Project or a part of the Project.

11.3 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.

11.4 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 10, and Annex 2.

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

11.6 When the Recipient(s) has committed actions, which obviously violate the national laws of Georgia, or which obviously are contrary to the objectives specified under the STCU Agreement, the Center shall terminate the Project with immediate effectiveness upon written notification of termination to the Recipient. In this case, the Recipient(s) shall promptly return to the Center all payments and goods previously provided to the Recipient(s).

Article 12 - Amendments, Variations, or Additions

The provisions of the Agreement and its annexes may be amended or supplemented by means of a written agreement signed by authorized representatives of the Signatory Parties. However, operational changes in Annex 1, other than changes in the project manager, the institution, and the overall schedule, can be made by agreement between the Center and the Recipient(s) upon approval by Partner requested in accordance with applicable clauses of Annex 1.

Article 13 - Annexes

The Annexes are an integral part of the Agreement. They are:

Annex 1 - Work Plan

Annex 2 - Financial Provisions

Annex 3 -- Reports

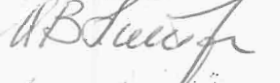
Annex 4 -- Intellectual Property

Article 14 - Entry into Force of the Agreement

The Agreement shall enter into force on the first of the month following the date this Agreement is signed by the last signature of Signatory Parties or the date Partner deposited its commitment in accordance with Article 3.6 to Center's account, whichever is later, i.e. on "the Operative Commencement Date".

Prepared in Kyiv in the English and Ukrainian languages (Russian optional, if the project is located only in other CIS State). In the event of inconsistencies between the English and other texts, the English text shall take precedence.

For the Center

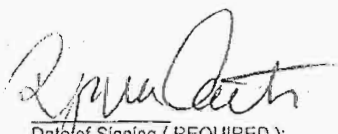

Igor Lytvynov

Date of Signing (REQUIRED):

22-11-2011

Andrew Hood
Executive Director
Science and Technology Center in
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For the Partner

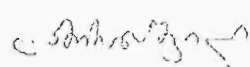


Date of Signing (REQUIRED):

15-11-2011

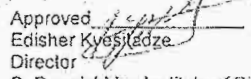
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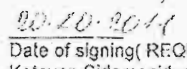
For the Recipient(s)

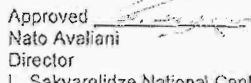

19-08-2011

Date of Signing (REQUIRED):

Lia Amiranashvili
Project manager

Approved  19-08-2011
Edisher Kyevladze
Director
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20-10-2011
Date of signing (REQUIRED):
Ketevan Sidamonidze
Project Manager

Approved  20-10-2011
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Annex I - Work Plan

1. Project Title P509

Isolation and characterization of probiotics that selectively grow on milk oligosaccharides

2. Project management

2.1 Project Manager:

Name: Amiranashvili Lia Luarsab (PhD)
Title: Senior Researcher
Institution: S. Durmishidze Institute of Biochemistry and Biotechnology of NLE Agrarian University of Georgia
Phone: (+995.32) 2528411
Fax: (+995.32) 2528026
E-mail: amiranashvili@hotmail.com

2.2 Name of leading institution/address:

Name: S. Durmishidze Institute of Biochemistry and Biotechnology of NLE Agrarian University of Georgia
Address: 0159, 10 km David Agmashenebeli Kheivani, Tbilisi, Georgia
Phone: (+995.32) 2528411
Fax: (+995.32) 2528026
E-mail: kvesitadze@hotmail.com

2.3 Name of participating institution(s)/addresses:

Name: L. Sakvarelidze National Center for Disease Control and Public Health
Address: 0177, 9, M.Asatiani St, Tbilisi, Georgia
Phone: (+995.32) 2398946
Fax: (+995.32) 2311485
E-mail: Nata.Avaliani@ncdc.ge

2.3.1 Participating institution Manager:

Name: Sidamonidze Ketevan Merab (Specialist)
Title: Chief Researcher
Institution: L. Sakvarelidze National Center for Disease Control and Public Health
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Fax: (+995.32) 2311485
E-mail: keti_sida@yahoo.com

2.4 Technical Monitor (partner's designee to oversee project progress, review project reports and other deliverables):

Institution: Lawrence Berkeley National Laboratory
Name: Tamas Torok
Phone: (+1.510) 4865808
Fax: (+1.510) 4865172
Address: Berkeley, California 94720, United States of America
E-mail: ttorok@lbl.gov

3. Introduction and Overview

Normal microbiota of intestines is one of the barriers on the way of exogenic infections; it participates in limitation of propagation of toxicogenic bacteria and in neutralization of the formed toxins.

Disorders in composition and functions of normal microbiota (dysbacteriosis) are developed in patients with pathologies of gastroenterological tract of inflectional and non-inflectional origin, during the viral and bacterial infections of non-intestinal localization, chronicle influential and allergic and radiation diseases, oenological patients and on the background of taking antimicrobial preparations and antibiotics.

On the background of dysbacteriosis, conditional pathogenic microorganisms, which cause intestinal diseases on penetrating into the organism, propagate rapidly in small and large intestines and display strong antagonism against own microbiota. The influential process is developed which in its turn is accompanied by interfering of short-chain fatty acids formation. Normal microbiota of large intestines protects immunocompetent cells of mucous membranes determining rapid response on infection. In addition, intestinal bacteria form biologically active compounds, which participate in regulation of homeostasis in the process of viability.

Probiotics and prebiotics are frequently employed to promote intestinal health and wellness. The presence of beneficial bacteria such as lactobacilli and bifidobacteria, whether delivered exogenously as probiotics or enriched via prebiotics, has been linked to positive health effects including reduction of gut inflammation, diarrhea, and allergic reactions.

What's the objective?

The goal is to develop a panel of probiotic strains that could be delivered in conjunction with milk oligosaccharides, as a single symbiotic application, to enhance intestinal persistence and probiotic efficacy.

What's the problem?

Milk oligosaccharides—naturally evolved prebiotics

The selective pressures that have refined milk's bioactive properties through the millennia are reflected in the benefits to the infant that offset the significant cost exacted from the mother during lactation. Whereas milk's role in enhancing mammalian fitness is inexorably linked to its nutritive value, milk's dual function as a delivery vehicle for bioactive agents to the infant gut cannot be ignored. Among the bioactive molecular constituents of milk, the oligosaccharide fraction is found in greater abundance in human milk than from bovine sources. These oligosaccharides represent the third most prevalent class of molecules besides lactose and fat (1). Human MOs (HMOs) are incorporated into the milk matrix with atypical structures that are recalcitrant to degradation by enzymes encountered in the gastrointestinal tract (GIT) (2). HMOs are composed of monomeric glucose, galactose, N-acetylglucosamine, fucose and sialic acid residues via 13 potential glycosidic bonds to generate structures containing 3 to 32 units. As each HMO species may represent several structural isomers, the potential for unique structures may be much higher (3). HMOs are believed to function to deflect pathogens by mimicking epithelial binding sites and also as

prebiotic substrates that facilitate bifidobacterial enrichment and interaction with the host (4). Numerous studies have demonstrated the dominance of bifidobacterial species in the feces of breast-fed infants as compared to formula-fed infants (5).

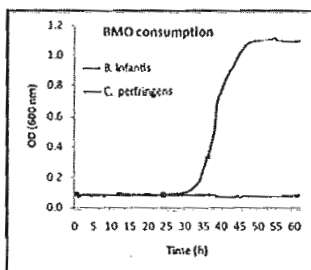


Figure 1. Growth of *B. infantis* and *Clostridium perfringens* on BMO.

What are other people doing?

Work from the UC Davis Functional Glycobiology Program (FGP; <http://fgp.ucdavis.edu/>) has shown that HMOs are used by select gut bacteria (*Bifidobacterium* and *Bacteroides* species) among the few tested to date (6). We have also demonstrated that only select species of bifidobacteria can consume human MOs (7, 8). Furthermore, we

demonstrated that small mass MO species are uniquely consumed by *Bifidobacterium longum* subsp. *infantis* (9). Genomic analysis of *B. infantis* isolates has revealed unique gene clusters linked to HMO metabolism that are specifically induced during growth on HMOs but are not expressed in cells grown on lactose or other prebiotics such as fructooligosaccharides (FOS), inulin, or galacto-oligosaccharides (GOS) (10). Bovine milk is known to contain small amounts of short oligomeric glycans, including sialylactose which is known to have established bioactive functions (11, 12). However, it has been long assumed that the concentration of these bioactive oligosaccharides was too low in bovine milk to warrant much interest. Moreover, evaluation of bovine MOs (BMOs) as a substitute for HMOs has been hindered by the lack of precise analytical methods to accurately identify and quantify these glycans. Recent advancements in MS-based glycan analyses at the UC Davis FGP have enabled accurate quantification of HMOs and BMOs (7, 11, 13-16). In turn, these analytical methods have enabled us to identify and characterize BMO-rich fractions isolated from dairy streams. Structurally, BMOs share many similarities to HMOs, and therefore are predicted to be resistant to human gastric enzymes and arrive intact in the GIT to be selectively metabolized in the colon by a bifidobacterial microbiota. Preliminary studies have shown that BMOs are selective for infant-borne bifidobacteria, such as *Bifidobacterium infantis*, and do not enable growth of the pathogen *Clostridium perfringens* (Figure 1). Clinical isolates of facultative anaerobes *Salmonella enterica* serovar Typhimurium and *Vibrio cholerae* also lack the ability to metabolize BMOs. Thus, BMOs promote the growth of a primary beneficial infant-borne bacterium without metabolic enhancement to three pathogenic agents, two of which cause considerable morbidity in infants and children.

What are we going to do?

This proposal seeks to identify and characterize LAB, bifidobacterial and yeast isolates from Georgia that grow on these BMOs as a sole sugar source.

- **Microbial profiling of raw milk fermentations**

Activity 1: Culture-based approach, strain ID, phenotypic and genotypic analyses

Raw milk fermentations will be identified by collaborators and samples collected at the end of fermentation stored on ice and transported to the host laboratory. Lactic acid bacteria and yeasts will be enumerated and isolated from these samples using standard methods. Isolates will be scored for each fermentation type (goat, bison, sheep milk). Species identity for bacteria will be determined by API strip analyses and partial 16S rDNA sequencing while yeasts will be identified using partial 26S rDNA sequencing. The collected isolates from the milks will then be scored for growth on BMO on agar plates using MRS (LAB) or YM (yeast) media supplemented with BMO as the sole fermentable sugar source and stored at -80°C.

Activity 2: Non-culture based approach

To characterize the full microbial diversity present, DNA will be directly purified from these fermentation samples and sent to LBNL. 16S and 26S rDNA amplicon pyrosequencing and data processing will be performed by the Joint Genome Institute. JGI has established 454 pyrosequencing of the 16S rRNA gene and other targets from fecal sample DNA extracts as a cost-effective approach to measure microbial diversity in the gut and quantify relative abundances of competing organisms.

- **Bifidobacterial isolations**

Activity: Identification of glycan consuming bifidobacteria

Bifidobacteria will be obtained from feces from breast-fed infants, as well as children and adults, who actively consume raw milk fermented products. Fecal matter will be diluted into 1 ml of Reinforced Clostridial Media (RCM) and plated on *Bifidobacterium* selective agar containing BMO as a sole sugar source. Agar plates will be incubated anaerobically (anaerobic jars with gas packs) at 37°C for 72 h. To analyze the dominant *Bifidobacterium* population of each subject, about 100 to 200 colonies (20 to 30 colonies from each plate), chosen based on different morphologies and sizes, will be randomly selected from each sample, and subcultured for 48 h in MRS and stored at -80°C.

- **Characterization of promising BMO-consuming probiotic candidates**

Examine the microbial diversity generated in Task 1 and 2 for various probiotic activities, including growth on BMOs (and other prebiotic sugars), production/characterization of bacteriocins, acid and bile tolerances

What's new?

Georgia is distinguished by its various natural conditions, variety of soil-climatic zones and biodiversity; consequently, it is rich in traditional dairy products. Lactic acid bacteria and propionic bacteria naturally present in dairy products; they participate in formation of taste properties of mentioned products (buttermilk, rendered butter, the liquid after cheese processing, cottage cheese, cards sour cream, precipitate of rendered butter whey, etc.).

This proposal will identify and screen putative probiotic microbial strains using a novel approach based on milk oligosaccharides as a means for enrichment, isolation, and efficacy.

2.5 Organization, Qualification and Staffing

Who we are

S. Durmishidze Institute of Biochemistry and Biotechnology of NLE Agrarian University of Georgia
(Director of the Institute, Professor Edisher Kvesitadze, phone/fax: +99532 528026, E-mail: kvesitadze@hotmail.com)

Founded in 1971. Main research activities:

- Creation of collection of microorganisms of different taxonomic groups from the diverse soil-climatic zones of the Caucasus with special attention to extremophiles. To date collection of microorganisms accounts up to 10.000 strains: microscopic fungi, bacteria, actinobacteria, including extremophiles - thermophiles, alkaliphiles, acidophiles, halophiles
- Selection of industrially valuable microbial strains (mutant, fusant and transformant) of different taxonomic groups, actively producing different enzymes and low-molecular-weight metabolites (citric acid, amino acids, etc) and enzymes (cellulases, xylanases, proteases, laccases, Mn-dependent peroxidases, etc). Among mesophilic and extremophilic fungi there are more than 400 strains active producers of cellulases),
- Investigation of plants and microorganisms ability to absorb and enzymatically degrade organic pollutants of different structure.
- Study of plant-bacteria-bacteriophage interactions; isolation and study of bacteriophage; Biological control of plant bacterial diseases.
- Study of the genome of higher plants and microorganisms.
- Investigation of rich endemic vegetation of the Caucasus on the content of physiologically active compounds. Isolation and characterization of these compounds. Evaluation of their potential commercial application.

Presently there are 85 co-workers. Above 150 publications. 1-USA, 1-Germany, 2-Swiss, 20-USSR, 5-Georgian Patents. 7 books, 2 in English (Springer), 3 in Russian (Nauka), 2 in Georgian languages. Participation in above 60 International meetings (since 2000).

Project participants have been involved in the projects as followed:

- Targeted Discovery of Lignocellulose-Deconstructing Enzymes from Extremophilic Fungi. STCU P433 2010-2012.
- New technology of complex phytoremediation of soils on basis of biosurfactants and biodiesel plants. STCU #4784. 2010-2012.
- Bacteriophage, an effective biological tool against plant diseases caused by pathogenic bacteria. ISTC #G-1129. 2005-2008.
- Biopreparation against tomato bacterial spot. GNSF-STCU. 2009-2011.

- Complex monitoring of military sites in Georgia ISTC G#564. 2003-2005.
- Creation of a novel complex phytoremediation technology for rehabilitation of soils and waters polluted with explosives. ISTC G-1408. 2008-2010.
- Development of a novel, cost-effective bioprocess for production of fuel ethanol from herbaceous lignocellulosic wastes. ISTC. G-1624. 2009-2011.
- Development of technologies of basidiomycetes ligninolytic enzymes production, dyes decolorization and TNT polluted soil bioremediation. STCU #3740. 2006-2009.
- Elaboration of a new strategy of phytoremediation and long-term protection of the environment polluted by hydrocarbons. ISTC #G-718.2002-2004.
- Elaboration of Methods of Bioremediation of Contaminated Soils on Former Military Locations and Proving Grounds in Georgia. ISTC, #G-369 2001-2004.
- Establishment of a Biotechnological Network of Regional Microbial Culture Collections in the Caucasus. CRDF_SCCRP, SCI-010002-SC-05. 2007-2008.
- Microbial diversity for novel biotechnology applications. IPP project STCU #P-196. Partner Project. Financed by DOE. Partner LBNL, USA. Technical monitor Dr.Tamas Torok. 2005-2008.
- Creation of collection of extremophilic mycelial fungi isolated from all ecological niches of the Caucasus, investigation their pathogenicity and elaboration of the technologies based on their degradational, oxidizing and synthesizing potential. STCU # G-101.2003-2006.
- Novel approach for the improvement of ecological guarantee of oil pipelines. STCU #3802. 2006-2009
- Selection of indigenous yeast strains capable of pesticides detoxification, their genetic analysis and application to obtain ecologically clean wine materials. GNSF/ST 08/8-497. 2009-2012.
- Prolongation of Expected Life Span and Improvement of Life Quality Basing on the Experience of Caucasian Longevity and Georgian Traditional Medicine. ISTC #G-895. 2004-2007
- Development of a Policy Framework on Cardiovascular Diseases Prevention Strategies in Georgia. NGO ACTS Georgia, Supported by Open Society Institute Regional Medical Program and Open Society – Georgia Foundation. 1998-1999.

Project Participants will do in the project:

Amiranashvili L. Ph.D, graduated from Tbilisi State University, Department of Biology. Responsible for general management of the project: preparation of quarterly and annual reports. Participation in microbiological research.

Kvesitadze G. Doctor of Biological Sciences, professor, Academician of Georgian National Academy of Sciences, graduated from Tbilisi State University, Department of Chemistry, Head of the Department of Biotechnology of DIBB. Biotechnologist. Great experience in microbial diversity. Enzyme hydrolases, oxidases and synthetases. Will be scientific leader of the project. Will coordinate works between two participating Institutes. Cooperation with Project partner and Technical Monitor.

Sadunishvili T. Doctor of Sciences, professor, graduated from Tbilisi State University, Department of Biology. Biochemist. In the frame of the project will be involved in Molecular Biology Research, organization of seminars, participation in meetings.

Gagelidze N. Ph.D. Graduated from Tbilisi State University, Department of Biology. Microbiologist. Experienced in selection and investigation of bacteria and yeasts. In the frame of the project will be Leader of Microbiology group. Culture-based approach, strain ID, phenotypic analyses. Identification of glycan consuming bifidobacteria. Examine the microbial diversity for various probiotic activities, including growth on BMOs, production/characterization of bacteriocins, acid and bile tolerances.

Kirtadze E. Doctor of Sciences, professor, graduated from Georgian State Agrarian University. In the frame of the project will be Consultant in research of bacteria and yeasts.

Gamkrelidze M. Ph.D. Graduated from Kutaisi State University. Faculty of Biology. In the frame of the project will be involved in Molecular Biology Research,

Varsimashvili Kh. Ph.D. Graduated from Tbilisi State University, Department of Biology.

Microbiologist. Will be involved in microbiological research. Isolation and characterization of bacteria and yeasts strains. Sample collection and procession. Culture-based approach, strain ID, phenotypic analyses. Identification of glycan consuming bifidobacteria. Examine the microbial diversity for various probiotic activities, including growth on BMOs, production/characterization of bacteriocins, acid and bile tolerances.

Tinikashvili L. Ph.D. Graduated from Tbilisi State University, Department of Biology. Geneticist. In the frame of the project will be involved in microbiological and molecular Biology researches. Isolation of

bacteria and yeasts strains. Sample collection and procession. Culture-based approach, strain ID, phenotypic and genotypic analyses.

Tataradze R. MD, PhD, Associate Professor. Graduated from Tbilisi State Medical Institute. In the frame of the project will be involved in data collection and analysis.

Chkhaidze Z. PhD. Graduated from Tbilisi State Medical Institute, General Doctor. In the frame of the project will be involved in data collection and analysis.

Mdivani K. Engineer. Graduated from Georgian Polytechnic Institute. In the frame of the project will be support person.

Selected Publications by project participants:

1. **Amiranashvili L., N. Gagelidze, Kh. Varsimashvili, L. Tinikashvili, E. Kirtadze.** The Collection of *Saccharomyces* Strains Isolated from the Different Soil-Climatic Zones of Eastern Georgia. 33rd World Congress of Vine and Wine. 20-25 June, 2010 Tbilisi, Georgia
2. **Kirtadze E., Papunidze G., Kvesitadze G.** Transformation of Wine Materials in the Process of Secondary Alcoholic Fermentation. 33rd World Congress of Vine and Wine. 20-25 June, 2010 Tbilisi, Georgia
3. **Gagelidze N., Kh. Varsimashvili, L. Amiranashvili, E. Kirtadze.** Introduction of 2,4,6-trinitrotoluene-degrading bacteria for the intensification of contaminated soils bioremediation process. *Annals of Agrarian Science*. 7, 3, 38-42, 2009
4. **Kirtadze E., Nutsidze N.** Metabolic potential of alcoholic fermentation yeasts. *Bulletin of the Georgian National Academy of Sciences*. 3, 1, 110-116, 2009
5. **Amiranashvili L. L., Gagelidze N. A., Jimsheleishvili T. E., Sachaneli T. Z., Zuroshvili L. D., Varsimashvili Kh. I., Tinikashvili L. M.** Selection of Bacteria Degrading Sodium Pentachlorophenolate. *Annals of Agrarian Science*. 7, 2, 75-79, 2009.
6. **Amiranashvili L., N. Gagelidze, L. Tinikashvili, Kh. Varsimashvili, E. Kirtadze, T. Torok, G. Kvesitadze.** Intensification of Mineral Oil Degradation Process in Soil by Introduction of *Rhodococcus* sp. strains. *Journal of Biological Physics and Chemistry*. 8, 73-77, 2008
7. **Sadunishvili T., Torok T., Kutateladze L., Gagelidze N., Pataria D., Kvesitadze E.** Collection of extremophilic microorganisms from the area of Caucasus source for stable enzymes. *Proceedings of the International Workshop: Plant and microbial enzymes: isolation, characterization and biotechnology applications*. 2-5 July, 2007, Tbilisi, Georgia. p. 79-84.
8. **Chkhaidze Z.** Nutritional load as a new test of atherosclerosis aggravation in elderly. *Experimental and Clinical Medicine*. 2007
9. **Kvesitadze, G., Khatisashvili, G., Sadunishvili, T., Ramsden, J.J.** Biochemical Mechanisms of Detoxification in Higher Plants. *Basis of Phytoremediation*. 262p. Springer, 2006.
10. **Kvesitadze G., T. Torok, L. Kutateladze, N. Gagelidze, L. Amiranashvili, E. Kvesitadze, E. Kirtadze, E. Kachlishvili.** Collection of bacteria and filamentous fungi isolated from different soil-climatic zones in the Southern Caucasus. *Proceedings of the annual general meeting of the European Culture Collections' Organization (ECCO XXV) "The role of culture collections at the beginning of the XXIst century"*. Budapest, Hungary, June 7-10, 2006, p.93-106
11. **Brotons C., Bjorkelind C., Bulc M., Ciurana R., Goducki-Cwirko M., Jurgova E., Kloppe P., Lionis C., Mierzecki A., Pineiro R., Pullerits L., Sammut SR, Sheehan M., Tataradze R., Thireos EA, Vuchak J.** Prevention and health promotion in clinical practice: the views of general practitioners in Europe. *Preventive Medicine* 40, 595-601, 2005
12. **Chkhaidze Z.** Aspects of ageing in Georgian traditional medicine. *Georgian Medical News*. 2005
13. **Elly P.H. Best, G. Kvesitadze, G. Khatisashvili, T. Sadunishvili.** Plant processes important for the transformation and degradation of explosives contaminants. *Zeitschrift für Naturforschung* 60c, 340-348, 2005.
14. **Navaro Peran E., Cabezas-Herrera J., Hiner A.N.P., Sadunishvili T. Garcia-Canovas F., Rodrigues-Lopez J.N.** Kinetics of the inhibition of bovine liver dihydrofolate reductase by tea catechins: origin of slow-binding inhibition and pH studies. *Biochemistry*, 44, 20, 7512 -7525, 2005.
15. **Tataradze R., K. Nadaraia, K. Liliashvili, M. Okujava, C. Aladashvili, N. Nodia, N. Mebonia, L. Sturua, T. Chachava, I. Kalandadze, K. Kiknadze, M. Parulava.** Smoking related behaviors on the example of adult population of Tbilisi [in Georgian]. *Cardiology and Internal Medicine XXI. Scientific-Practical Journal (Tbilisi)*. 3, 105-110, 2003
16. **Kvesitadze, G. I., Kvachadze, L. L., E. G. Kvesitadze,** Selection of thermophilic cellulase-producing micromycetes. *Appl. Biochem. Microbiol.* 33, 132-137, 1997

L. Sakvarelidze National Center for Disease Control and Public Health (NCDC) of Georgia is a primary national public health center responsible for public health surveillance and response of communicable and non communicable diseases. NCDC was built on the foundation of the Georgian Station for Plague Control, established in 1937; Research Center for Especially Dangerous Pathogens since 1992; NCDC

with integrated epidemiological units from SES since 1996; Integration of Center of Medical Statistics with the NCDC in 2003; Integration of the functions of MoH Public Health Department to the NCDC in 2007.

The main activities and responsibilities of the Center includes: surveillance and control of infectious and non infectious diseases, control and prevention of public health diseases, outbreak investigations, IHR National Focal Point, National Immunization Programme, National Referral Laboratories; National Repository of EDP's, Medical statistics; Health promotion; Training and continuing education; Ensuring biosecurity and biosafety, development of didactic and regulatory documents on surveillance, control and prevention of diseases; collection and exchange of information inside and outside of the country. Communicable diseases surveillance guidelines are developed and implemented based on the WHO recommendations (USAID funded project). They cover VPDs, diarrheal diseases, viral hepatitis, meningitis, and rabies and include: standard case definitions; case registration, notification, reporting requirements, data analysis; case/outbreak investigation and response; feedback and supervision of surveillance activities; protocols for sample collection, storage, and transportation for laboratory investigation.

In addition to rapid detection and response to outbreaks NCDC carry out molecular-epidemiological investigation and characterization of especially dangerous and other newly isolated pathogens compared them with stored in the Live Culture Museum. Various molecular diagnostic and typing techniques are used like PCR, Real-Time PCR, Nested PCR, RAPD; IS-fingerprinting, PFGE, MLVA, RFLP, SNP, Sequencing.

International Collaboration:

- WHO- Sentinel Surveillance of Rotavirus Gastroenteritis; Sentinel Surveillance of Meningitis Laboratory Surveillance for Measles-Rubella; Laboratory Surveillance for Polio
- CDC - Surveillance and Response of Avian and Pandemic Influenza
- GFATM - Consolidation of achievements: Prevent Malaria Epidemic
- GAVI - Implement of pentavalent vaccines, enhancing the System
- VRF - Hepatitis B prevalence in Pregnant and Medical Workers
- BP - Monitoring of Pipeline Rout Epidemiological Situation
- NAMRU 3, DOD/DTRA - Laboratory Research of Fever Diseases
- DSTL, UK - Cell mediated-Immunity of Brucellosis
- EU/UNDP -Tobacco, Alcohol and Other Drugs Use in Georgian Students; pilot study rigorously following criteria of ESPAD
- UNFPA, UNICEF, USAID, CDC- Reproductive Health Survey (2000, 2005, 2010)
- USAID/Save the Children-US, Georgia Field Office - Nutritional Status of Children Under Five Years of Age in Six Regions of Georgia 2000-2001
- UNICEF -Georgia National Nutrition Survey 2009
- DHHS, CDC - Southern Caucasus Field Epidemiology and Laboratory Training Program
- UNIVERSITY of PATRAS, Greece – Iodine Deficiency survey
- EU TACIS - PRIMARY HEALTH CARE REFORM SUPPORT PROJECT
- Development of the Health Promotion Strategy and Implementation plan;
- Implementing standardized population behaviour risk-factor survey using WHO's STEPS instrument/methodology and analysis framework.

Completed and ongoing joint research projects at the NCDC:

- International Training and Research in Emerging Infectious Diseases – Fogarthy Center, NIH; University of Maryland , Baltimore, SUNY, Albany, NY
- Enhanced Epidemiologic and Laboratory Diagnostic Capacity for the Control of Botulinum Intoxication. Collaborator: CDC, Atlanta, GA.
- Prevention of Amebiasis and Creation of Diagnostic Test-Systems for *E. histolytica* Strains Isolated in Georgia. Collaborator: University of Virginia Health System, Charlottesville, VA.
- Molecular Epidemiology and Antibiotic-Resistance of Bacterial Infections. Collaborator: University of Maryland, Baltimore, MD.
- Clinical and Molecular Epidemiology of Drug-Resistant Tuberculosis in Georgia and the Caucasus.

- Collaborator: Emory University, Atlanta, GA.
- Epidemiology, Molecular Characteristics and Clinical Course of HCV Infection. Collaborator: Johns Hopkins University, Baltimore, MD.
- Epidemiological, Clinical and Microbiological Studies of *Helicobacter pylori* Infection and Public Health Diagnosis and Treatment to Reduce Burden of Clinical Illness. Collaborator: CDC, Atlanta, GA.
- Development of Surveillance System and Control Strategy for Leishmaniasis in Georgia by means of Epidemiological Investigation and Strengthening Laboratory Capacities. Collaborator: NIAID, Bethesda, MD.
- Improvement of Hospital Infection Control Practice in Georgia through Fundamental Change in the Medical Role and Economic Structure of Microbiology. Collaborator: Minnesota Department of Health, Minneapolis.
- Application of Molecular Fingerprinting to Geographical Characterization and Epidemiological Surveillance of Natural foci of *Yersinia pestis* and *Francisella tularensis*. Collaborator: Lawrence Livermore National Laboratory, Livermore, CA.
- Clinical and Molecular Epidemiology of Meningitis Caused by Enteroviruses. Collaborator: CDC, Atlanta, GA.
- Salmonella Surveillance in Georgia. Collaborator: CDC, Atlanta, GA.
- Diagnostics, Laboratory and Epidemiological Assessment of Brucellosis in Georgia. Collaborators: U.S. Army Medical Institute of Infectious Diseases, Walter Reed Army Institute, Louisiana State University.

Sidamonidze Ketevan – Main Researcher, Division of Laboratory, NCDC.

Education and Qualification: 2002 – M.D., Tbilisi Medical Academy, 2003-2005 - Resident student, Tbilisi Medical Academy 2008-2009 - Laboratory Training at Mycotic and Parasitic diseases Laboratory, Wadsworth Center, Albany, NY, Fogarty Fellowship program, New York State International Training Program.

She was taken part in many projects (CRDF GG-17 “Clinical, epidemiological and laboratory Estimation of Brucellosis in Georgia” /2009-2011/, Global Fund Grant # GEO-607-G04-M, “To prevent malaria outbreaks, to reduce malaria morbidity and the number of active malaria foci, and to reduce potential threats caused by malaria /2007-2011/.

In the frame of the project she will be Project Manager.

Tevzadze Liana – Chief Researcher, Division of Laboratory, NCDC.

Education and Qualification: 1965 – M.D., Tbilisi State Medical Institute, 1981 – Ph.D, Tbilisi State Medical Institute. 2004 - WHO Training course in intestinal infections, Moscow, Russia, 2005, 2006, 2007 - WHO Training course in intestinal infections, St.Petersburg, Russia

She was take part in many projects (BTEP, ISTC-1195 “Epidemiological, Clinical and Microbiological studies of *Helicobacter pylori* Infection and Public Health Diagnosis and Treatment to reduce Burden of clinical illness” /2006-2009/, BTEP/ ISTC G-1462, “Establishment of national sentinel-site, laboratory-based Salmonella surveillance system and outbreak response capacity for enhanced control of foodborne disease in the Republic of Georgia” /2007-2011/ and etc.).

In the frame of the project she will be Head of Microbiological Team.

Kekelidze Merab – Chief Researcher, Department of Laboratory, NCDC.

Education and Qualification: 1978 – M.S. Biology, Tbilisi State University; 1978-1981 – M.S. Molecular Biology, Institute of Physiology of Academy of Sciences of Georgia; 1986 – Ph.D. Molecular Biology, Institute of Molecular Biology of Academy of Sciences of USSR, Moscow; 1998-1999 – Advanced studies, Molecular Biology, University of Maryland, Baltimore, US; 2003 – Advanced studies, Molecular Biology, Lawrence Livermore National Laboratory (LLNL), CA, USA

Work responsibilities: Molecular Fingerprinting of different infectious agents using PFGE, RAPD, PCR/ Real-Time PCR based MLVA and SNP methodologies.

He was take part in many scientific projects (G-597, BTEP / ISTC - “Molecular Epidemiology and Antibiotic-Resistance of Bacterial Infections in Georgia” /2002-2005/; P-142a, STCU, “Application of Molecular Fingerprinting to Geographical Characterization and Epidemiological Surveillance of Natural foci of *Yersinia pestis* and *Francisella tularensis* in the Republic of Georgia”/2006-2007/; G-1462, DHHS

BTEP/ISTC, Establishment of National Sentinel-Site, Laboratory-Based Salmonella Surveillance System and Outbreak Response Capacity for Enhanced Control of Foodborne Disease in the Republic of Georgia" /2007-2010/ and etc.).

In the frame of the project he will be Head of Molecular Biology Team.

Imnadze Paata – Head of Scientific Board, NCDC. He is Professor and Head of Department of Public Health, Tbilisi State University.

Education and Qualification: 1976 – M.D., Tbilisi State Medical University; 1983 – Ph.D., Tbilisi State Medical University. Nov.1997-March.1998 - Research Associate-University of Maryland, Baltimore, US. He has 38 Conference Papers & Presentations, 76 Scientific Publications and 3 textbooks. He was take part in many scientific projects. Prof. Imnadze has several honours (1987 - Central Institute of Postgraduate Training for Doctors at the Ministry of Health USSR, Award for graduating of Management Course for Health Leadership, Moscow. 1995 - CDC Award for International Publications Management Course, Atlanta, US. 1999 - University of Minnesota; International Infection Control Institute. 2001 - University of Minnesota; Summer Institute on International Public Health Topics. 2003 - Georgian State Order of Dignity).

Memberships: 1994-pres. Member Elect, Academician of Georgian Academy of Sciences of Preventive Medicine. 1999-pres Member of Board, Georgian Association of Public Health; 2001-2004 Member of the Society for Healthcare Epidemiology of America; 2003-2006 Member from WHO European Region – Joint Coordinating Board, UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases; 2004-pres Vice President, Scientific Association of Infectious Diseases, Parasitic Diseases, Epidemiology and Microbiology of Georgia; 2005-pres Member of the WHO European Technical Advisory Group of Experts on Immunization; 2006 Member of Editorial Board of the WHO policy document "Essential elements for the development of intersectoral Food Safety Strategies in Europe".

In the frame of the project he will be Group Leader.

Tsereteli David – Chief Researcher, Division of Outbreak and Bioterrorism Response, NCDC.

Education and Qualification: 1989 – M.D., Tbilisi State Medical University; 1994 – Ph.D., Tbilisi State Medical University; 1990 - Postgraduate Education, Moscow Medical Academy; June, 2005 – Caroline University, Stockholm, Sweden.

Dr. David Tsereteli studies epidemiology of communicable and non-communicable diseases. During the period of the former USSR Dr. Tsereteli worked in Georgian Anti-plaque Station, which worked on secret projects. He has 21 Conference Papers & Presentations, 56 Scientific Publications and 3 textbooks. Dr. Tsereteli has several awards and grants from international organization (European Societies of Chemotherapy, 2nd European Congress of Chemotherapy and 7th Biennial Conference on Antiinfective Agents and Chemotherapy /May 8-11, 1998, Hamburg/. European Society of Clinical Microbiology and Infectious diseases, 9th European Congress of Clinical Microbiology and Infectious Diseases /March 21-24, 1999, Berlin/. British Society for Antimicrobial Chemotherapy - Young Investigators Award, 21st International Congress of Chemotherapy /4-9 July 1999, Birmingham/. European Society of Clinical Microbiology and Infectious diseases, 10th European Congress of Clinical Microbiology and Infectious Diseases, /May 28-31, 2000, Stockholm/. Federation of European Societies of Chemotherapy and Infection Award, 3rd European Congress of Chemotherapy /May 7-10, 2000. Madrid/. American Cancer Society, RITC, CTCRI /2004/ and etc.).

He was take part in many scientific projects (ISTC/BTEP G-596 "Molecular Epidemiology and Antibiotic Resistance of Bacterial Infections in Georgia" /2002-2005/. ISTC/BTEP G-1059 "Improvement of Hospital Infection Control Practice in Georgia through Fundamental Change in the Medical Role and Economic Structure of Microbiology" /2005-208/, and etc.).

In the frame of the project he will be Head of Data Collection and Analysis Team.

Tvauri Irina – Bacteriologist

Education and Qualification: 1972 – B.A., Faculty Biology, Tbilisi State University, 2004-2005 - Bacteriology, Tbilisi State Medical Academy.

She was take part in many scientific projects (BTEP/ISTC G-1462 "Establishment of national sentinel-site, laboratory-based Salmonella surveillance system and outbreak response capacity for enhanced control of foodborne disease in the Republic of Georgia" /2007-2011/, BTEP/ISTC G-617 "Prevention of

Amebiasis and Creation of Diagnostic Test-Systems for *E. histolytica* Strains Isolated in Georgia" /2001-2005/.

In the frame of the project, she will carry out the following works: sample collection and microbiological Research.

Jintcharadze Manana – Bacteriologist

Education and Qualification: 1986 – B.A., Tbilisi State Veterinary Institute.

She was take part in many scientific projects (BTEP/ISTC G-1462 "Establishment of national sentinel-site, laboratory-based Salmonella surveillance system and outbreak response capacity for enhanced control of foodborne disease in the Republic of Georgia" /2007-2011/, BTEP/ISTC G-617 "Prevention of Amebiasis and Creation of Diagnostic Test-Systems for *E. histolytica* Strains Isolated in Georgia" /2001-2005/.

In the frame of the project, she will carry out the following works: sample collection and microbiological Research.

Ganiashvili Tamar – Senior Researcher, Department of Laboratory, NCDC.

Education and Qualification: 1997 -- M.S. Faculty of Biology and Medicine, Tbilisi State University.

2001 - Training Course of Bacteriology (Medical Academy of Postgraduate Education), 2002 - National Laboratory Capacity Strengthening, Communicable Disease Surveillance and Response Course in Lyon. (World Health Organization (WHO) Office in Lyon–CSR/LYO France), (First Course), 2003 - National Laboratory Capacity Strengthening, Communicable Disease Surveillance and Response Course in Lyon. (World Health Organization (WHO) Office in Lyon–CSR/LYO France), (Second Course), 2007 - Training course on National Laboratory management and quality control, Lyon, France (World Health Organization (WHO) Office in Lyon–CSR/LYO France), (Third Course), September 15–October 17, 2008 - Management for International Public Health (MIPH) course conducted by the Sustainable Management Development Program, U.S. Centers for Disease Control and Prevention (CDC), and the Rollins School of Public Health, Emory University. Atlanta, Georgia.

She was take part in many scientific projects (STCU P-142 "Application of molecular fingerprinting to geographical characterization and epidemiological surveillance of natural foci of *Yersinia pestis* and *Francisella tularensis* in the Republic of Georgia", BTEP, ISTC-1195 "Epidemiological, Clinical and Microbiological studies of Helicobacter Pylori Infection and Public Health Diagnosis and Treatment to reduce Burden of clinical illness" /2006-2009/, BTEP/ ISTC G-1462, "Establishment of national sentinel-site, laboratory-based Salmonella surveillance system and outbreak response capacity for enhanced control of foodborne disease in the Republic of Georgia" /2007-2011/).

In the frame of the project, she will carry out the following works: sample collection and microbiological Research.

Ramaz Shengelia – Medical Doctor.

Education and Qualification: 1975 – M.D., Tbilisi State Medical Institute, 1990 - High Courses of Moscow Semashko Scientific-Research Institute of Health Organization and Social Hygiene.

He was take part in scientific project Prolongation of Expected Life Span and Improvement of Life Quality Basing on the Experience of Caucasian Longevity and Georgian Traditional Medicine (ISTC-EU) /2004-2007/.

In the frame of the project, he will carry out the following work: Data Analysis.

Zhgenti Ekaterine – Senior Researcher, Department of Laboratory, NCDC

Education and Qualification: 1998 – M.S. Biology Tbilisi State University; July-August, 2003 – Lawrence Livermore National Laboratory (LLNL), CA, USA; March, 2005 - Laboratory Training, US AFRIMS, Bangkok, Thailand; May, 2005 - Laboratory Training, US AMRIID, Tbilisi, Georgia; October, 2008 - Laboratory Training, London School of Hygiene & Tropical Medicine, London, UK

Work responsibilities: Molecular Diagnostic and Fingerprinting of different infectious agents using PCR, Real-Time PCR, PFGE, RAPD, MLVA, SNP methodologies.

She was take part in many scientific projects (G-597, BTEP / ISTC - "Molecular Epidemiology and Antibiotic-Resistance of Bacterial Infections in Georgia" /2002-2005/; P-142a, STCU, "Application of Molecular Fingerprinting to Geographical Characterization and Epidemiological Surveillance of Natural foci of *Yersinia pestis* and *Francisella tularensis* in the Republic of Georgia"/2006-2007/ and etc).

In the frame of the project she will carry out the following work: Molecular Biology Research.

Guram Katsitadze – Member of Scientific Board, NCDC

Education and Qualification: 1958 – M.D., Tbilisi State Medical Institute, 1964 – Ph.D., Tbilisi State Medical Institute, 1973 - Doctor of Science, Tbilisi State Medical Institute.

He was take part in many scientific projects (STCU P-142 “Application of molecular fingerprinting to geographical characterization and epidemiological surveillance of natural foci of *Yersinia pestis* and *Francisella tularensis* in the Republic of Georgia”, CRDF GG-17 “Clinical, epidemiological and laboratory Estimation of Brucellosis in Georgia” /2009-2011/ and etc.).

In the frame of the project he will be scientific consultant.

Selected Publications by project participants:

1. Chitadze N., Kuchuloria T., Clark D.V., Tsertsvadze E., Chokheli M., Tsertsvadze N., Trapaidze N., Lane A., Bakanidze L., Tsanava S., Hepburn M.J., **Imnadze P.** Hantavirus Infection in the Republic of Georgia; Emerging Infectious Diseases, Vol. 15, No. 9, September 2009, 1489-91.
2. Revazishvili T., Rajanna C., Bakanidze L., Tsertvadze N., **Imnadze P.** Characterization of *Yersinia pestis* isolates from Foci of Plague in the Republic of Georgia, and their Relationship to *Y.pestis* Isolates from Other Countries; Clin Microbiol Infect 2008; 14: 429-436.
3. Burjanadze I., Kurtsikashvili I., **Tsereteli D., Imnadze P.,** Rhame F., Besser J., Toscano R. O’Boyle C. Pseudomonas aeruginosa infection in an intensive care unit. International Journal of Infection Control, 2007; Vol 3, No 2; 1-3.
4. **Imnadze P.,** Tsertsvadze N., Velijanashvili I., Kukhalashvili T., Beridze L., Bakanidze L., **Tsereteli D., Kekelidze M.** Plague in Georgia. Plague: Epidemics and Societies. Firenze University Press. 2007; 23-25.
5. Sami L. Gottlieb, K. Kretsinger, N. Tarkhashvili, N. Chakvetadze, M.Chokheli, M. Chubinidze, R. Hoekstra, E Jhorjholiani, M.Mirtskhulava, M. Moistsrapishvili, M. Sikharulidze, T Zardiashvili, **P. Imnadze,** and Jeremy Sobel; Long-Term Outcomes of 217 Botulism Cases in the Republic of Georgia; Clinical Infectious Diseases, 2007, v. 45, 174 -180;
6. Revazishvili T., Bakanidze L., Gomelauri T., **Zhgenti E., Chanturia G., Kekelidze M., Rajanna C., Kreger A., Sulakvelidze A.** Genetic background and antibiotic resistance of Staphylococcus aureus strains isolated in the Republic of Georgia. Journal of Clinical Microbiology, October 2006, p. 3477-3483, Vol. 44, No. 10
7. G.Rotas, K.Natchkebia, N.Natsvlshvili, **M.Kekelidze,** A.Kimbaris, G.Varvounisand, D.Mikeladze, Action of a novel pyrrol[1,2-c][1.3]benzodiazepine on the viability of Jurkat and neuronal/glia cells; Bioorganic & Medicinal Chemistry Letters, Vol. 15, Issue 13, 1 July 2005, Pages 3220-3223
8. Bakanidze L., Velijanashvili I., **Kekelidze M.,** Beridze L., Zangaladze E., Zakalashvili M., **Tsereteli D., Imnadze P.** Polymerase Chain Reaction Assays for the Presumptive Identification of Yersinia pestis Strains in Georgia; in: Advances in Experimental Medicine and Biology, Vol. 529, The Genus Yersinia: Entering the Functional Genomic Era, Kluwer Academic/Plenum Publishers, 2003, p. 333-336.
9. **Tsereteli D.,** Bakanidze L., Velijanashvili I., Beridze L., Manrikyan M., Shakhikyan M., Kekelidze M., Zangaladze E., Tsertvadze N., **Imnadze P.** Plague in Southern Caucasus. Antibiotika Monitor. Austria. 2002; Vol. XVIII. P.14-16.
10. **Imnadze P.,** Bakanidze L., Manrikyan M., Kukhalashvili T., Zangaladze E., Kekelidze M., **Tsereteli D.,** Nadiradze M., Tsanava Sh., Tsertvadze N. Anthrax in Southern Caucasus. Antibiotika Monitor. Austria. 2002; Vol. XVIII. P.17-18.
11. Sulakvelidze A., **Kekelidze M.,** Turabelidze D., Tsanava S., **Tevsadge L.,** Devdariani L., Gautom R., Myers R., J. G. Morris, Jr., and **P. Imnadze.** 2000. Salmonellosis in the Republic of Georgia: Using Molecular Typing to Identify the Outbreak-causing Strain. Emerg Infect Dis. 1:70-73.
12. Sulakvelidze, A., **M. Kekelidze,** T. Gomelauri, Y. Deng, N. Khetsuriani, K. Kobaidze, A. De Zoysa, A. Efstratiou, J. G. Morris, Jr., and **P. Imnadze.** 1999. Diphtheria in the Republic of Georgia: use of molecular typing techniques for characterization of Corynebacterium diphtheriae strains. J. Clin. Microbiol.10: 3265-3270.

4. Expected Results

In addition to quarterly progress reports to be delivered in accordance with Article 4, the following technical schedule activities/events are considered the deliverables under the Agreement:

Deliverables	Due date (by the end of Month)	Point (address) of delivery
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	#)	
Large number (>500) of BMO-consuming strains and purified DNA from samples.	12	Tamas Torok, Lawrence Berkeley National Laboratory. 1 Cyclotron Road Street q, Berkeley, California, USA, 94720
Large number (>500) of BMO consuming strains	21	Tamas Torok, Lawrence Berkeley National Laboratory. 1 Cyclotron Road Street q, Berkeley, California, USA, 94720
Technical report on isolated, identified, and profiled the diversity of Lactic acid bacteria and yeasts present in traditional raw milk (goat, bison, sheep milk) fermentations;	24	Tamas Torok, Lawrence Berkeley National Laboratory. 1 Cyclotron Road Street q, Berkeley, California, USA, 94720
Technical report on glycan-consuming <i>bifidobacteria</i> ..	24	Tamas Torok, Lawrence Berkeley National Laboratory. 1 Cyclotron Road Street q, Berkeley, California, USA, 94720
Technical report on Characterized probiotic candidates according to acid and bile tolerance, and growth on BMO, DSM-OS and glycoprofiling.	24	Tamas Torok, Lawrence Berkeley National Laboratory. 1 Cyclotron Road Street q, Berkeley, California, USA, 94720

The implementation of this research will lead to:

- Identification and characterization of lactic acid bacteria, bifidobacterial and yeast isolates from Georgia that grow on bovine milk oligosaccharides (BMOs) as a sole sugar source;
- Selection of candidate strains that grow well on BMO and DSM-OS and exhibit favorable/interesting phenotypes (bile/acid tolerance and antimicrobial production);
- Generation draft genomic data for the most promising probiotics obtained;
- Applied modern molecular techniques will be implemented at DIBB and NCDC Molecular biology laboratories for conducting lactic acid bacteria and bifidobacteria study.

5. Scope of Activities

General description of the activities within the project. Detailed description for each task follows.

Task 1

Task description and main milestones	Participating Institutions
Microbial profiling of raw milk fermentations <i>Activity 1: Culture-based approach, strain ID, phenotypic and genotypic analyses</i> Raw milk fermentations will be identified by collaborators and samples collected at the end of fermentation stored on ice and transported to the host laboratory. Lactic acid bacteria and yeasts will be enumerated and isolated from these samples using standard methods. Isolates will be scored for each fermentation type (goat, bison, sheep milk). Species identity for bacteria will be determined by API strip analyses and partial 16S rDNA sequencing while yeasts will be identified using partial 26S rDNA sequencing. The collected isolates from the milks will then be scored for growth on BMO on agar plates using MRS (LAB) or YM (yeast) media supplemented with BMO as the sole fermentable sugar source and stored at -80°C. <i>Activity 2: Non-culture based approach</i> To characterize the full microbial diversity present, DNA will be directly purified from these fermentation samples and sent to LBNL. 16S and 26S rDNA amplicon pyrosequencing and data processing will be performed by the Joint Genome Institute. JGI has established 454 pyrosequencing of the 16S rRNA gene and other targets from fecal sample DNA extracts as a cost-effective approach to measure microbial diversity in the gut and quantify relative abundances of competing organisms. Milestones: Large number (>500) of BMO-consuming strains available, paper on microbial ecology of raw milk fermentations.	1. S. Durmishidze Institute of Biochemistry and Biotechnology of NLE Agrarian University of Georgia 2. National Center for Disease Control and Public Health

Task 2

Task description and main milestones	Participating Institutions
Bifidobacterial isolations <i>Activity: Identification of glycan consuming bifidobacteria</i> Bifidobacteria will be obtained from feces from breast-fed infants, as well as children and adults, who actively consume raw milk fermented products. Fecal matter will be diluted into 1 ml of Reinforced Clostridial Media (RCM) and plated on <i>Bifidobacterium</i> selective agar containing BMO as a sole sugar source. Agar plates will be incubated anaerobically (anaerobic jars with gas packs) at 37°C for 72 h. To analyze the dominant <i>Bifidobacterium</i> population of each subject, about 100 to 200 colonies (20 to 30 colonies from each plate), chosen based on different morphologies and sizes, will be randomly selected from each sample, and subcultured for 48 h in MRS and stored at -80°C. Milestones: Large number (>500) of BMO consuming strains available.	1. S. Durmishidze Institute of Biochemistry and Biotechnology of NLE Agrarian University of Georgia 2. National Center for Disease Control and Public Health

Task 3

Task description and main milestones	Participating Institutions
Characterization of promising BMO-consuming probiotic candidates Examine the microbial diversity generated in Task 1 and 2 for various probiotic activities, including growth on BMOs (and other prebiotic sugars), production/characterization of bacteriocins, acid and bile tolerances Milestones: Identification of promising probiotic candidates.	1. S. Durmishidze Institute of Biochemistry and Biotechnology of NLE Agrarian University of Georgia 2. National Center for Disease Control and Public Health

6. Technical Approach and Methodology

Specific Aim 1. Profile microbial diversity from small scale goat, sheep, and bison raw milk fermentations.

We hypothesize that food grade microorganisms isolated from sheep, goat, or bison milk fermentations common to the Caucasus region represent an ideal pool for screening growth on BMOs and probiotic bioactivity. This is due to two reasons: first, these raw milk fermentations are carried out by indigenous microbes (LAB, bifidobacteria, and yeasts) present in the milk. A second reason is that the fermented milks produced in this region are often made from sheep, goat, or bison milk. These milks have been shown to contain significantly more complex oligosaccharides than observed in common commercial, feedlot-generated bovine milks (11, 12, 17). As a consequence we believe that the indigenous microbes that carry out these fermentations are more likely to encounter and consume complex MOs and thus, represent a more diverse pool of microbes than has been examined to date.

The goal of this aim is to isolate, identify, and profile the diversity of LAB and yeasts present in these traditional raw milk fermentations. Our hypothesis is that since non-bovine milks contain higher amounts of complex oligosaccharides (degree of polymerization >3), these fermentations will more likely contain food grade microbes that are capable of growth on complex HMOs and BMOs. We will only sample at the end of these fermentations since it would be expected that lactose, the predominant sugar in milk, would be the main energy source driving the initial stages of the milk fermentations.

Culture-based methods: Indigenous microbiota from 50 raw milk fermentations, each in Armenia and Georgia will be characterized by culture-based and non-culture based methods. Raw milk fermentations will be identified by collaborators and samples collected at the end of fermentation stored on ice and transported to the host laboratory. Lactic acid bacteria and yeasts will be enumerated and isolated from these samples using standard methods (18). Isolates will be scored for each fermentation type (goat, bison, sheep milk). Species identity for bacteria will be determined by API strip analyses and partial 16S

rDNA sequencing (19) while yeasts will be identified using partial 26S rDNA sequencing (20). The collected isolates from the milks will then be scored for growth on BMO on agar plates using MRS (LAB) or YM (yeast) media supplemented with BMO as the sole fermentable sugar source and stored at -80°C.

Non-culture based methods: To characterize the full microbial diversity present, DNA will be directly purified from these fermentation samples using methods described previously (21) and sent to LBNL. 16S and 26S rDNA amplicon pyrosequencing and data processing will be performed by the Joint Genome Institute. JGI has established 454 pyrosequencing of the 16S rRNA gene and other targets from fecal sample DNA extracts as a cost-effective approach to measure microbial diversity in the gut (22) and quantify relative abundances of competing organisms (23).

Taxonomy-based analyses will be performed by assigning taxonomic status to each sequence using a modified version of the CLASSIFIER program of the Ribosomal Database Project (24). To test for milk-type and regional effects on species richness and diversity, rarefaction and Shannon's diversity estimates will be developed from phylogeny-based analysis of the data. Operational Taxonomic Units (OTU) will be defined using a combination of CD-Hit to generate clusters, followed by alignment of representative sequences from robust clusters using Infernal Aligner. Based on the alignment, clusters with 97% identity in representative sequences will be pooled into OTUs. Milk-type and regional effects on the entire microbiota will also be examined using the Unifrac method (25) which measures relative distances of microbial populations based on specific branch lengths in de-replicated phylogenetic trees. Ultimately, we will test for correlation between the different milk-type and regional parameters and the quantitative estimates of individual bacterial taxa (taxonomy-based) or OTUs (phylogeny-based) from the rDNA data.

Specific Aim 2: Isolate bifidobacteria from feces of infants, children, and adults, who consume raw milk products.

Bifidobacteria will be obtained from feces from breast-fed infants, as well as children and adults, who actively consume raw milk fermented products. Fecal matter will be diluted into 1 ml of Reinforced Clostridial Media (RCM) and plated on *Bifidobacterium* selective (26) agar containing BMO as a sole sugar source. Agar plates will be incubated anaerobically (anaerobic jars with gas packs) at 37°C for 72 h. To analyze the dominant *Bifidobacterium* population of each subject, about 100 to 200 colonies (20 to 30 colonies from each plate), chosen based on different morphologies and sizes, will be randomly selected from each sample, and subcultured for 48 h in MRS and stored at -80°C. Once the isolates have been stored they will be regrown on agar plates and characterized by partial 16S rDNA sequencing (19) to determine species ID.

Specific Aim 3. Examine the microbial diversity generated in Aim 1 and 2 for various probiotic activities including growth on BMOs (and other prebiotic sugars), production/characterization of bacteriocins, acid and bile tolerances.

Isolates obtained from Aims 1 and 2 will be screened for growth on various prebiotic sugars including (inulin, FOS, GOS), as well as a proprietary oligosaccharide provided by DSM, the US industrial partner (termed DSM-OS). Isolates will be further screened for antimicrobial (bacteriocin) production using a simple agar diffusion assay (27). In addition, bile and acid tolerances of these isolates determination will be determined using standard assays (28, 29).

Candidate strains that grow well on BMO and DSM-OS and exhibit favorable/interesting phenotypes (bile/acid tolerance and antimicrobial production) will be sent to UC Davis for further BMO growth rate determination and, in select cases, analysis of the oligosaccharides consumed, as described elsewhere (7).

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7. Project Location and Facilities

Institution	Location, Facilities and Equipment
Leading Institution	Durmishidze Institute of Biochemistry and Biotechnology of NLE Agrarian University of Georgia 0159, Georgia, Tbilisi, 10th km, David Agmasheneblis kheivani. The work will be carried out in laboratories located in Rooms #301, 305, 407-411, and in the shaker room of Institute. Total area of laboratory premises: 220 m². Following equipment is available for experimental and research activities: centrifuges - K-23 and K-24, microcentrifuge (Eppendorf), Spectrophotometer UV/VIS (JENWAY 650), laminar box (LKB), autoclaves, thermostats, microscope, refrigerators, Ultra low freezer-800C (Revco), Freeze Dryer 250L. Micro Modulyo 230, Vial Cell stoppering shelf F05623000; Vacuum Pump; Thermo. pH-meter (Mi 150 MARTINI), balances: electric (Nahita) and technical, Horizontal electrophoresis apparatus (Thermo), Thermostate U10, Thermocycler (TC-412, TECHNE), Shaker (Vortex GENIE 2), etc.
Participant Institution 1	National Center for Disease Control and Public Health Address: 9, M. Asatiani st., Tbilisi, 0177, Georgia The work will be carried out in laboratories located in rooms #202, 204, 504, 506 and 510. Total area of laboratory premises: 235 m². The following equipment is available for experimental and research activities: Biological Safety Cabinet, Class II, type 2A/B3 Incubators Refrigerators Termocycler GENIUS, Techne Light Cycler 2.0, Roche Thermo-mixer, Eppendorf Ultracentrifuge Centrifuge Electrophoresis apparatus Gel documentation and analysis system Pulse field gel electrophoresis horizontal apparatus Capillary Electrophoresis System, DNA Sequencer CEQ 8000

	Beckman Coulter Spectrophotometer Genesys 10, Thermo Scientific
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8. Financial Information

Table 1 presents Work schedule specified for each participating institution as identified by I-Code.
Table 2 presents Work schedule chart.

Budget categories (allowable direct cost) are specified in the following tables:

Grant payments: Table 3

Equipment: Table 4

Materials: Table 5

ODC: Table 6

Travel: Table 7

Tables 8 and 9 present financial summary including overhead for participation institutions.
Tables S8 and S8 present financial summary for each participating institution separately.

Table 2. Work Schedule Chart / Jadwal 2. Durapasa etnis nepcoy

Stage number	Beginning date	Duration, month	Q1					Q2					Q3					Q4					Q5					Q6					Q7					Q8					Q9					Q10					Q11					Q12				
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36																								
1 Stage	1	24	Maximum retention of new and old candidates																																																											
2 Stage	1	24	Initial candidate selection																																																											
3 Stage	1	12	Characterization of remaining 50% - examining preliminary candidates																																																											
4 Stage			FNU																																																											
5 Stage			FNU																																																											
6 Stage			FNU																																																											
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Table 5. Materials / Таблица 5. Матеріали

[illegible]

Table 7. Travel / Таблиця 7. Відвідування

#	Country of Destination	City	Inst.	People	Institute of Destination	Purpose of Travel	V-code	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Total
International																				
1	USA	Berkeley	2	5	Lawrence Berkeley National Laboratory	Developed study instruments, experiments, and protocols.	C	13000	0	0	0	0	0	0	0	0	0	0	0	13000
2	USA	Berkeley	2	2	Lawrence Berkeley National Laboratory	Train on sequencing. Information exchange and discussion of results.	C	0	0	0	0	7000	0	0	0	0	0	0	0	7000
3	USA	Denver	2	4	National Science Foundation	Participation in 11th General Meeting, May 15-21, 2013, Denver, Colorado	C	0	0	0	0	0	0	9400	0	0	0	0	0	9400
4	USA	Berkeley	1	1	Berkeley, Livermore	Information exchange and discussion of results.	C	0	0	0	0	4000	0	0	0	0	0	0	0	4000
5	USA	Denver	1	2	Conference	Participation at the conference	C	0	0	0	0	0	0	5000	0	0	0	0	0	5000
Total International Costs:								13000	0	0	0	11000	0	14400	0	0	0	0	0	38400
Domestic																				
1	Georgia	Istumi, Zugdidi etc.	2	4	Regions of Georgia	Sample collection	C	760	0	760	750	500	600	320	0	0	0	0	0	3790
2	Georgia	Istumi, Zugdidi etc.	1	4	Distant regions of Georgia	Sample collection	C	1000	0	0	1320	850	0	450	0	0	0	0	0	3620
Total Domestic Costs:								1760	0	760	2070	1350	600	780	0	0	0	0	0	7230

Summary	
International:	38400
Domestic:	7230
Total:	45730

Table 8. Financial Summary / Таблиця 8. Зведена фінансова інформація

#	Item	Qtr1	Qtr2	Qtr3	Qtr4	Qtr5	Qtr6	Qtr7	Qtr8	Qtr9	Qtr10	Qtr11	Qtr12	Total
1	Days - FWS	306	308	310	310	304	304	303	293	0	0	0	0	2 438
2	Days - NFWS	175	188	195	196	208	208	208	206	0	0	0	0	1 584
	Total Days:	481	496	505	506	512	512	511	499	0	0	0	0	4 022
1	Grants - FWS	13290	13320	13385	13390	14205	14230	14165	13855	0	0	0	0	109 840
2	Grants - NFWS	5725	6175	6420	6450	6820	6820	6820	6760	0	0	0	0	51 990
3	Grants total:	19015	19495	19805	19840	21025	21050	20985	20615	0	0	0	0	161 830
4	Equipment	5300	0	0	0	0	0	0	0	0	0	0	0	5 300
5	Materials	18690	2000	0	3256	11044	0	0	0	0	0	0	0	34 990
6	Other Direct Costs	348	325	325	805	312	310	2342	302	0	0	0	0	5 070
7	Travel International	13000	0	0	0	11000	0	14400	0	0	0	0	0	38 400
8	Travel Domestic	1760	0	760	2080	1350	600	780	0	0	0	0	0	7 330
9	Travel Total:	14760	0	760	2080	12350	600	15180	0	0	0	0	0	45 730
10	Non-Labor Expenses:	39098	2326	1085	6141	23706	910	17522	302	0	0	0	0	91 090
11	Total Expenses:	58113	21821	20890	25981	44731	21960	38507	20917	0	0	0	0	252920
12	Overhead for the Institution	3510	510	510	510	510	510	510	510	0	0	0	0	7080
13	Total Project Cost:	61 623	22 331	21 400	26 491	45 241	22 470	39 017	21 427	0	0	0	0	260 000

Overhead for the Institution(s): 2.8
Project duration (quarters): 8

STCU fee - 5% 0
STCU fee -0% - for this case delete 5 in a cell above
Total Project Cost 260 000

Table 9. Financial Summary (Cumulative)

#	Item	Qtr1	Qtr2	Qtr3	Qtr4	Qtr5	Qtr6	Qtr7	Qtr8	Qtr9	Qtr10	Qtr11	Qtr12
1	Days - FWS	306	614	924	1234	1538	1842	2145	2438	2438	2438	2438	2438
2	Days - NFWS	175	363	558	754	962	1170	1378	1584	1584	1584	1584	1584
	Total Days:	481	977	1482	1988	2500	3012	3523	4022	4022	4022	4022	4022
1	Grants - FWS	13290	26610	39995	53385	67590	81820	95985	109840	109840	109840	109840	109840
2	Grants - NFWS	5725	11900	18320	24770	31590	38410	45230	51990	51990	51990	51990	51990
3	Grants total:	19015	38510	58315	78155	99180	120230	141215	161830	161830	161830	161830	161830
4	Equipment	5300	5300	5300	5300	5300	5300	5300	5300	5300	5300	5300	5300
5	Materials	18690	20690	20690	23946	34990	34990	34990	34990	34990	34990	34990	34990
7	Other Direct Costs	348	674	999	1804	2116	2426	4768	5070	5070	5070	5070	5070
8	Travel International	13000	13000	13000	13000	24000	24000	38400	38400	38400	38400	38400	38400
9	Travel Domestic	1760	1760	2520	4600	5950	6550	7330	7330	7330	7330	7330	7330
10	Travel Total:	14760	14760	15520	17600	29950	30550	45730	45730	45730	45730	45730	45730
11	Non-Labor Expenses:	39098	41424	42509	48650	72356	73266	90788	91090	91090	91090	91090	91090
12	Total Expenses:	58113	79934	100824	126805	171536	193496	232003	252920	252920	252920	252920	252920
13	Overhead for the Institution	3510	4020	4530	5040	5550	6060	6570	7080	7080	7080	7080	7080
14	Total Project Cost:	61 623	83 954	105 354	131 845	177 086	199 556	238 573	260 000	260 000	260 000	260 000	260 000

S8. Estimated expenditures by each participating institution / Кошторисні витрати організацій-учасників

S. Durmashidze Institute of Biochemistry and Biotechnology of NLE Agrarian University of Georgia														Overhead 0%
#	Item	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Total
1	Days - FWS	180	180	181	181	183	158	158	158	158	0	0	0	1335
2	Days - NFWS	81	81	81	81	81	81	81	81	81	0	0	0	848
	Total Days:	261	261	262	262	240	240	239	240	240	0	0	0	2048
1	Grants - FWS	8230	8230	8270	8278	8250	8278	8210	8278	0	0	0	0	66018
2	Grants - NFWS	2250	2250	2250	2250	2250	2250	2250	2250	0	0	0	0	18000
3	Grants total:	10480	10480	10520	10528	10500	10528	10460	10528	0	0	0	0	84018
4	Equipment	3720	0	0	0	0	0	0	0	0	0	0	0	3720
5	Materials	9180	0	0	0	3790	0	0	0	0	0	0	0	12880
6	OtherDirectCosts	280	280	280	760	280	280	1215	280	0	0	0	0	3655
7	Travel International	0	0	0	0	4000	0	5000	0	0	0	0	0	9000
8	Travel Domestic	1000	0	0	1330	850	0	450	0	0	0	0	0	3630
9	Travel Total	1000	0	0	1330	4850	0	5450	0	0	0	0	0	12630
10	Non-Labor Expenses	14180	280	280	2090	8930	280	6685	280	0	0	0	0	32965
11	Total Expenses	24670	10760	10600	12613	19420	10606	17123	10605	0	0	0	0	117000
12	Overhead	3000	0	0	0	0	0	0	0	0	0	0	0	3000
13	Total project cost	27670	10760	10600	12613	19420	10606	17123	10605	0	0	0	0	120000

L. Sakavarefide National Center for Disease Control and Public Health													Overhead 3%	
#	Item	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Total
1	Days - FWS	126	126	126	126	145	145	145	134	0	0	0	0	1081
2	Days - NFWS	84	107	114	115	127	127	127	125	0	0	0	0	938
	Total Days:	220	235	243	244	272	272	272	259	0	0	0	0	2017
1	Grants - FWS	5065	5090	5115	5115	5665	5655	5665	5550	0	0	0	0	43825
2	Grants - NFWS	3475	3923	4170	4200	4570	4570	4570	4510	0	0	0	0	33590
3	Grants total:	8535	9015	9285	9315	10525	10525	10525	10060	0	0	0	0	77815
4	Equipment	1580	0	0	0	0	0	0	0	0	0	0	0	1580
5	Materials	9500	2000	0	3256	7254	0	0	0	0	0	0	0	22010
6	Other Direct Costs	68	48	45	45	32	36	1127	22	0	0	0	0	1415
7	Travel International	13000	0	0	0	7000	0	9400	0	0	0	0	0	29400
8	Travel Domestic	760	0	760	750	500	600	330	0	0	0	0	0	3700
9	Travel Total	13760	0	760	750	7500	600	9730	0	0	0	0	0	33100
10	Non Labor Expenses	24902	2049	805	4051	14766	830	10857	22	0	0	0	0	58105
11	Total Expenses	33443	11061	10090	13365	25311	11350	21382	10112	0	0	0	0	135920
12	Overhead	510	510	510	510	510	510	510	510	0	0	0	0	4080
13	Total project cost	33953	11571	10600	13874	25821	11665	21892	10622	0	0	0	0	146000

[illegible][illegible]

Table S9. Cumulative expenditures by each participating institution / Витрати організацій-учасників із зростаючим підсумком

S. Durmishidze Institute of Biochemistry and Biotechnology of NLE Agrarian University of Georgia													
#	Item	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12
1	Days - FWS	180	368	541	722	881	1040	1198	1357	1357	1357	1357	1357
2	Days - NFWS	81	162	243	324	405	486	567	648	648	648	648	648
	Total Days:	261	522	784	1046	1286	1526	1765	2005	2005	2005	2005	2005
1	Grants - FWS	8230	16460	24730	33000	41250	49630	57740	66015	66015	66015	66015	66015
2	Grants - NFWS	2250	4500	6750	9000	11250	13500	15750	18000	18000	18000	18000	18000
3	Grants total:	10480	20960	31480	42000	52500	63030	73490	84015	84015	84015	84015	84015
4	Equipment	3720	3720	3720	3720	3720	3720	3720	3720	3720	3720	3720	3720
5	Materials	9190	9190	9190	9190	12980	12980	12980	12980	12980	12980	12980	12980
6	OtherDirectCosts	280	560	840	1600	1880	2180	3375	3655	3655	3655	3655	3655
7	Travel International	0	0	0	0	4000	4000	8000	9000	9000	9000	9000	9000
8	Travel Domestic	1000	1000	1000	2330	3180	3180	3630	3630	3630	3630	3630	3630
9	Travel Total:	1000	1000	1000	2330	7180	7180	12630	12630	12630	12630	12630	12630
10	Non-Labor Expenses	14180	14470	14750	16840	25760	26040	32705	32985	32985	32985	32985	32985
11	Total Expenses	26470	34530	46230	58845	78600	106195	117000	117000	117000	117000	117000	117000
12	Overhead	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
13	Total project cost	27670	38430	49230	61845	81265	92070	109195	120000	120000	120000	120000	120000

L. Sakvarelidze National Center for Disease Control and Public Health													
#	Item	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12
1	Days - FWS	126	254	383	512	657	802	947	1081	1081	1081	1081	1081
2	Days - NFWs	94	201	315	430	557	684	811	936	936	936	936	936
	Total Days:	220	455	698	942	1214	1486	1758	2017	2017	2017	2017	2017

1	Grants - FWS	5060	10150	15265	20380	26335	32290	38245	43825	43825	43825	43825	43825
2	Grants - NFWFS	3475	7400	11570	15770	20340	24910	29480	33990	33990	33990	33990	33990
3		Grants total:	8535	17550	26835	36150	46675	57200	67725	77815	77815	77815	77815
4	Equipment	1580	1580	1580	1580	1580	1580	1580	1580	1580	1580	1580	1580
5	Materials	9500	11500	11500	14758	22010	22010	22010	22010	22010	22010	22010	22010
6	OtherDirectCosts	68	114	159	204	236	266	1393	1415	1415	1415	1415	1415
7	Travel International	13000	13000	13000	13000	20000	20000	29400	29400	29400	29400	29400	29400
8	Travel Domestic	760	760	1520	2270	2770	3370	3700	3700	3700	3700	3700	3700
9		Travel Total:	13760	13760	14520	15270	22770	23370	33100	33100	33100	33100	33100
10	Non-Labor Expenses	24908	26554	27759	31810	40596	47226	58083	58105	58105	58105	58105	58105
11		Total Expenses	43453	44504	54594	67960	93271	104428	125808	135920	135920	135920	135920
12	Overhead		510	1020	1530	2040	2550	3060	3570	4080	4080	4080	4080
13	Total project cost		33953	45524	56124	70000	95821	107488	129378	140000	140000	140000	140000

[illegible][illegible]

Annex 2 - Financial Provisions

Article 1 - Allowable Costs

1.1 Costs shall include actual costs incurred for the Project after the operative commencement date which are necessary for the performance of the project. Allowable costs may only include the cost categories defined in Articles 2 and 3 of this annex.

1.2 The original estimates of expenditures set forth in Annex I may be adjusted by the project manager between categories in consultation with the Center and Partner, and provided that the transfers do not fundamentally alter the scope or content of the project.

Article 2 - Direct Costs

2.1 Personnel

2.1.1 Personnel costs may be charged to the project as direct costs.

2.1.2 The institution and the project manager are responsible for certifying the times devoted to the Project by the individual participants, as reflected in project time cards prepared by individual participants. Personnel costs charged to the Project shall be in increments of one hour.

2.1.3 The project manager may increase the time commitments of personnel by up to 10 percent during one quarter of any individual without approval of the Center but may not change the daily rate without approval of the Center. The project manager may request more significant changes in personnel commitments, including changes in the names of personnel, at the beginning of each quarter. Such significant changes must be fully justified in writing. Changes in scientific personnel must provide for the new individual participants to have technical credentials and previous weapons experience comparable to those of the individual participants they replace. The Center, in consultation with the Partner, will respond promptly to such requests.

2.1.4 The Center will not pay personnel costs associated with holidays, vacations, overtime, or sick leave. Such additional costs, if any, are the responsibility of the Recipient(s).

2.1.5 Since the individual participants will remain employees of the institution, the Center's act of direct grant payments to the individual participants will not transfer from the Recipient(s) to 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.

2.1.6 The Recipient(s) 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.

2.1.7 Individual participants must personally record the hours worked on STCU projects on time cards according to the following procedures:

Project Manager and Participating Institution Manager Responsibilities

Project managers and Participating Institution Managers are required to do the following:

- i. Provide project participants with a separate time card for each STCU project that they will work on. Each time card must contain a project number.
- ii. Ensure that project participants understand which time card must be used to record hours worked on each project.
- iii. Ensure that all project participants correctly record the hours worked on STCU projects according to the procedure described in the project participant responsibilities section below.
- iv. Transmit completed time cards to the STCU no later than the 10th of each month.
- v. Control blank time cards provided by the STCU.
- vi. Certify that the hours recorded on the time cards are true and accurate by signing them.
- vii. Obtain signatures of two other project participants on their own (project managers' and participating institution managers') time cards in addition to their own signature.

Project Participant Responsibilities

Project participants are required to do the following:

- i. Complete a separate time card for each STCU project that they work on. Time cards are for a period of one month.
- ii. Personally complete their time cards **each working day and in ink.**

- iii. Correct time cards by crossing out mistakes and inserting the correct information on the next line; no erasures may be made to time cards. Project workers must initial the corrections.
- iv. Sign their own time cards at the end of each month.
- v. Certify, on an as needed basis, that the hours recorded on the time cards of the project manager or participating institution manager are true and accurate by signing their cards.

2.1.8 Payments to individual participants will be based on properly completed time cards as described in Section 2.1.7 above

2.1.9 The Center will provide blank time cards for use on this project. Such time cards will be printed on card stock and will be serially numbered. Only time cards provided by the Center may be used to record hours worked on STCU projects; photocopied time cards are not acceptable.

2.1.10 Project participation is limited as described in the STCU Standard Operating Procedure XXIV – Project Participation in STCU Projects: A copy of this procedure may be obtained on the STCU's website at the following address: <http://www.stcu.int/documents/reports/financial/>.

2.2 Equipment

2.2.1 The cost of equipment used in the project which is purchased, fabricated, or leased may be charged to the Project as a direct cost. The total lease costs may not exceed the purchase price of the equipment.

2.2.2 Equipment purchased in accordance with Article 3.3 of the Agreement will be preserved, accounted for, and maintained throughout the term of the Project by the Recipient(s).

2.2.3 . Equipment purchased for the project should be identified as described in the STCU Standard Operating Procedure XXIII - Identification Of Equipment Purchased For Stcu Projects. A copy of this procedure may be obtained on the STCU's website at the following address: <http://www.stcu.int/documents/reports/financial/>.

2.3 Materials

The costs of materials required for the Project shall be allowable costs.

2.4 Services and Other direct costs

2.4.1 Costs associated with (1) testing facilities, (2) computer services, (3) communication, (4) security services, (5) repairing/maintenance of equipment, (6) laboratory tests outside, (7) publications, and (8) patenting, but excluding items covered by Article 4 of Annex 2, may be charged as direct costs to the project through cost allocation formulas approved by the Center, provided such facilities and services contribute to the project and are accessible for monitoring and auditing in accordance with Article 9 of this agreement.

2.5 Travel and per diem

The following travel costs may be charged to the project:

- i. Airline Tickets. Reimbursement is limited to the cost of coach or economy class airfare by the most direct, cost-effective routing.
- ii. Train Tickets. Reimbursement for first class rail fare is authorized.
- iii. Lodging.
 - A. Within Country of Residence, reimbursement is limited to the lower of the actual cost or \$100.00 (taxes not included) per day.
 - B. Outside Country of Residence, reimbursement is limited to the lower of the actual cost or the maximum amount allowed in the U.S. Joint Travel Regulations (taxes not included). If lodging is pre-arranged for the traveler because of conference participation funded by the STCU, then the maximum amount allowed in the U.S. Joint Travel Regulations may be exceeded by up to 25% (taxes not included). In those exceptional cases where there are no accommodations available within the maximum amount allowed or accommodations are unacceptable, then the most cost-effective accommodation is authorized with prior approval of the responsible Deputy Executive Director. Maximum lodging rates outside of a country of

residence may be obtained from the STCU treasurer or at
<http://www.state.gov/m/a/als/prdm/xxxx>¹

- C. Lodging without receipt is not compensated.
- iv. Meals and Incidental Expenses (M&IE).
 - 1. Within Country of Residence, the M&IE is \$35.00 per day.
 - 2. Outside Country of Residence, the M&IE is \$50.00 per day.
- v. Other Costs. Actual cost of passports, visa, or conference registration is authorized with receipt. Withdrawal fees accepted by the STCU.
- vi. Use of Privately Owned Vehicle. Reimbursement for the use of a privately owned vehicle to perform travel is authorized at the rate of \$.10 per kilometer. Records must be kept for this activity, including destination and kilometers traveled, and odometer readings. Documents must be signed and approved by project manager.
- vii. Local Travel. Reimbursement for the actual cost of local travel (taxi, bus, etc.) is authorized. Receipts must be obtained.

2.5.1 Additional Travel and per diem information is contained in STCU Standard Operating Procedure V – Project Participants Travel. A copy of the this procedure may be obtained on the STCU's website at the following address: <http://www.stcu.int/documents/reports/financial/>.

Article 3 - Overhead

3.1 A fixed amount may be charged for project overhead to cover the cost of such items as general administration, institutional management, depreciation of buildings and equipment, maintenance, utilities, staff training or any other cost at discretion of the institute management.

3.2 The total fixed amount may not exceed 10 percent of total direct costs, exclusive of the cost of items provided in-kind by the Center.

3.3 One half of the direct overhead costs will be retained by the Center until project completion.

Article 4 - Costs not Allowed

4.1 Allowable costs shall not include: profit; contributions to pension, medical, or other social funds; provisions for possible future losses or liabilities; taxes, including profit tax, value added tax, personal income tax, local taxes, tariffs, dues, customs duties, import duties, or others; and costs allocable to another project.

Article 5 - Cash Payments by the Center

5.1 Within Ukraine, all cash payments will be made in the national currency of Ukraine. Conversion of US dollars or Euro to the national currency of Ukraine will be according to the exchange rate of the Interbank Rate of Ukraine. Within Azerbaijan, Georgia, Uzbekistan, and Moldova all cash payment will be made in U.S. Dollars or Euros where possible. The Center shall pay its financial contribution through special bank accounts established.

5.2 The Center shall pay the following financial contribution:

- (a) An advance payment, which is one third of the first quarter grant payment to the project grantees, as soon as possible following the operative commencement date;
- (b) Quarterly grant payments after approval by the Center of the cost statement for the last completed quarter and, upon Partner's request, after approval by the Partner the quarterly progress report.
- (c) Pursuant to Article 3.4, the Center shall make payments of overhead to the participating institutions represented by their respective directors as a fixed payment. One half of the allowable overhead will be paid to the Recipient(s) represented by its director after approval of progress and cost reports. Retention shall be made by the Center of 50% of the allowable overhead for the Recipient(s). The retention shall be released to the Recipient(s) represented by its director within one month following the approval by the Center of the last technical or financial document or other deliverable required by the Agreement.
- (d) Current payments directly to vendors in amounts, which are estimated in Annex 1. Such payments shall be based on vendor invoices and other documents delivered to the Center with written requests from the project manager.

¹ Where "xxxx" is the year the travel will begin. For example: 2004.

5.3 The Center shall make grant payments directly to private bank accounts of the project grantees in accordance (1) with Letters of agreement between the Center and with each project grantee and (2) payment level rates set forth in Annex 1 and the amount of time devoted to the project by each grantee as certified by the project manager.

5.4 If the Center 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.

5.5 If on completion or termination of the work, the payments made by the Center exceed the actual allowable costs, the Recipient(s) 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 and the unspent portion of the Total Cost of the Project will be returned to the Partner account.

5.6 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 to the Recipient(s) shall in principle be suspended as long as the suspension remains in effect.

5.7 If the Project is terminated, costs shall be limited to the allowable costs incurred by the Recipient(s) 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.

Article 6 - Project Accounting

The Recipient(s) shall maintain financial documentation, such as invoices, shipping documents and copies of time cards to support and justify the costs reported.

Article 7 - Timing of Financing

7.1 Funds will be disbursed when the partner has deposited the specified amount of its funding commitment to the partner activity, including the STCU fee. Funds are to be deposited in US dollars or Euro in the following account:

Commitment in USD:
Deutsche Bank Trust Company Americas, New York
Partner Contribution Account #04-406-956
Fedwire ABA #021001033
SWIFT BIC: BKTRUS33

Commitment in Euro:
Fortis Bank, Montagne du Park 3, B-1000 Brussels, Belgium
Account No. 210-0777641-44
IBAN: BE55 2100 7776 4144
SWIFT: GEBABEBB

7.2 Interest earned on partner funds will be retained by the STCU.

7.3 Partner will deposit its commitment in accordance with the following schedule

Payment	Due Date	Commitment to the total cost of the project	STCU fee	Total commitment
First payment	Before the Operative Commencement Date	131,845 USD	0	131,845 USD
Second Payment	Before the second year	128,155 USD		128,155 USD
Total		260,000 USD		260,000 USD

Annex 3 - Reports

Article 1 - Cost Statements

1.1. Quarterly cost statements covering each three-month period following the operative commencement date shall be submitted to the Center within 20 days after the end of each reporting period. The format for cost statements will be provided by the Center.

1.2 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.

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.

Article 2 - Reports

2.1 The Recipient shall submit the following reports:

(a) Quarterly progress reports covering each three-month period following the operative commencement date shall be submitted to the Center, to the Partner and/or to the Technical Monitor in accordance with Article 4 within one month after the end of each reporting period. The format for progress report will be provided by the Center.

(b) Technical reports, requested by the Partner, containing a description of the significant results according to the deliverables determined in the Annex I -- Work Plan, to be submitted to the Partner and/or to the Technical Monitor within one month after significant results are achieved.

(c) A final report covering all the work, the objectives, the results, and the conclusions, including a suitable summary of all these aspects shall be submitted to the Partner and/or to the Technical Monitor within two months of the completion of the Project work plan or termination of the Agreement, or the agreed completion date of the Agreement, whichever is the earliest. A suitable unrestricted summary of the final report shall be submitted to the Center.

2.2 It is the responsibility of the Recipient, in consultation with the Partner and/or with the Technical Monitor/, to indicate clearly what parts of reports contain invention or business confidential information and specify any limitations on circulation. For each report, 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

2.3 The Recipient shall submit any additional reports or any other deliverables requested by the Partner and/or by the Technical Monitor and specified in Annex 1.

Annex 4 – Intellectual Property

I. NOTICE AND ASSISTANCE REGARDING PATENT AND COPYRIGHT INFRINGEMENT.

Recipient shall report to the Partner, promptly and in reasonable written detail, each notice or claim of patent or copyright infringement based on the performance of this Project Agreement of which Recipient has knowledge and shall furnish to the Partner, at the expense of the Partner, when requested by the Partner, all evidence and information in possession of Recipient pertaining to such claim or any resulting suit.

II. PATENT RIGHTS.

(a) Definitions

- (1) "Subject Invention" means any invention or discovery of Recipient conceived or first actually reduced to practice in the performance of work under this Project Agreement.
- (2) "Patent Counsel" means the U.S. Department of Energy (DOE) Patent Counsel assisting the Partner.

(b) Invention disclosures and reports

- (1) Recipient shall furnish Center, the Technical Monitor, and Patent Counsel:
 - (i) A written report containing full and complete technical information concerning each Subject Invention within two months after conception or first actual reduction to practice, whichever occurs first, in the course of or under this Agreement, but in any event prior to any on sale, public use, or public disclosure of such invention known to Recipient. The report shall identify the Project Agreement and inventor and shall be sufficiently complete in technical detail and appropriately illustrated by sketch or diagram to convey to one skilled in the art to which the invention pertains a clear understanding of the nature, purpose, operation, and to the extent known, the physical, chemical, biological, or electrical characteristics of the invention.
 - (ii) Upon request, but not more than annually, interim reports on a DOE approved form listing Subject Inventions for that period and certifying that all Subject Inventions have been disclosed or that there were no such inventions; and
 - (iii) A final report on a DOE-approved form within 3 months after completion of the Project Agreement work listing all Subject Inventions and certifying that all Subject Inventions have been disclosed or that there were no such inventions.
- (2) Recipient agrees that the U.S. Government and the Technical Monitor may duplicate and disclose Subject Invention disclosures and all other reports and papers furnished or required to be furnished pursuant to this Project Agreement.

(c) Rights to Subject Inventions

- (1) In accordance with the STCU Statute, all rights worldwide to Subject Inventions belong to the Recipient. The Recipient and the Partner have agreed to protect and allocate such Subject Inventions as specified in paragraph (c)(2) below.
- (2) The Recipient has title to Subject Inventions in the New Independent States. Recipient hereby grants to the Technical Monitor the entire right, title and interest

to Subject Inventions in all countries other than the New Independent States. Recipient acknowledges the right of the Technical Monitor to file applications and execute all documents necessary to obtain patents in said countries. Subject Inventions jointly made by Recipient and the Technical Monitor shall be jointly owned.

- (3) Recipient acknowledges that Partner may obtain title to each Subject Invention for which a patent application or applications are not filed by Recipient or the Technical Monitor and for which any issued patents are not maintained by Recipient and the Technical Monitor. To the extent that Partner acquires title to a Subject Invention, Recipient agrees to take such actions and execute all appropriate documents (at no expense to Recipient) to enable Partner to file, prosecute and maintain patent applications thereon.
- (4) Recipient acknowledges that the U.S. Government retains a non-exclusive, nontransferable, irrevocable, paid-up license to practice or to have practiced by or on behalf of the U. S. Government every Subject Invention throughout the world.
- (5) Recipient certifies that it has not entered, and will not enter, into an agreement with a third party that conflicts with this Project Agreement. To the extent that any subsequent agreement between Recipient and a third party conflicts with the allocation of rights in Subject Inventions under this Project Agreement, Recipient agrees that the terms of the Project Agreement will supersede the terms of the subsequent agreement.

(d) Publication

In order that information concerning scientific or technical developments conceived or first actually reduced to practice in the course of or under the Agreement is not prematurely published so as to adversely affect patent interests of the Technical Monitor, Recipient agrees to submit to the Technical Monitor for patent review a copy of each paper 60 days prior to its intended publication date. Recipient may publish such information after a 60-day period following such submission or prior thereto if specifically approved by the Technical Monitor, unless Recipient is informed in writing within the 60-day period, that in order to protect patentable subject matter, publication must further be delayed. In this event, publication shall be delayed up to 100 days beyond the 60-day period or such longer period as mutually agreed.

(e) Royalty Sharing

To the extent that the Technical Monitor licenses any Subject Invention to a third party which results in income therefrom, Recipient and the Technical Monitor will share the net income therefrom fifty percent (50%) to Recipient and fifty percent (50%) to the Technical Monitor. Net income is gross income less any expenses and costs associated with the licensing of a Subject Invention including, but not limited to, the cost of preparing, prosecuting and maintaining patents covering said Subject Inventions. The Technical Monitor will provide to Recipient annual reports setting forth the licensing activity for Subject Inventions by the Technical Monitor during the reporting period. The Technical Monitor will provide that any agreement to license a Subject Invention will be subject to the royalty sharing arrangement between the Technical Monitor and Recipient

(f) Employee Agreements

Recipient shall obtain agreements to effectuate the provisions of this Patent Rights clause from all persons in its employ who perform any part of the work under this Project Agreement except non-technical personnel, such as clerical employees and manual laborers.

III. RIGHTS IN DATA - GENERAL

(a) Definitions

- (1) "Computer software," as used in this clause, means computer programs, computer databases, and documentation thereof.
- (2) "Data," as used in this clause, means recorded information, regardless of form or the media on which it may be recorded. The term includes technical data and computer software. The term does not include information incidental to contract administration, such as financial, administrative, cost or pricing, or management information.
- (3) "Form, fit, and function data," as used in this clause, means data relating to items, components, or processes that are sufficient to enable physical and functional interchangeability, as well as data identifying source, size, configuration, mating, and attachment characteristics, functional characteristics, and performance requirements; except that for computer software it means data identifying source, functional characteristics, and performance requirements but specifically excludes the source code, algorithm, process, formulae, and flow charts of the software.
- (4) "Limited rights data," as used in this clause, means data (other than computer software) developed at private expense that embody trade secrets or are commercial or financial and confidential or privileged.
- (5) "Technical data," as used in this clause, means data (other than computer software), which are of a scientific or technical nature.
- (6) "Restricted computer software," as used in this clause, means computer software developed at private expense and that is a trade secret; is commercial or financial and is confidential or privileged; or is published copyrighted computer software; including minor modifications of such computer software.
- (7) "Unlimited rights," as used in this clause, means the right of the U.S. Government to use, disclose, reproduce, prepare derivative works, distribute copies to the public, and perform publicly and display publicly, in any manner and for any purpose, and to have or permit others to do so.
- (8) "Limited rights," as used in this clause, means the rights of the U.S. Government and Partner in limited rights data as set forth in the Limited Rights Notice of paragraph (e)(2) of this clause.
- (9) "Restricted rights," as used in this clause, means the rights of the U.S. Government and Partner in restricted computer software, as set forth in the Restricted Rights Notice of paragraph (e)(3) of this clause.

(b) Allocations of rights

- (1) Except as provided in paragraph (c) below regarding copyright, Center, the U.S. Government and the Technical Monitor shall have unlimited rights in:

- (i) Data first produced in the performance of this Project Agreement;
 - (ii) Form, fit, and function data delivered under this Project Agreement;
 - (iii) Data delivered under this Project Agreement (except for restricted computer software) that constitute manuals or instructional and training material for installation, operation, or routine maintenance and repair items, components, or processes delivered or furnished for use under this Project Agreement; and
 - (iv) All other data delivered under this Project Agreement unless provided otherwise for limited rights data or restricted computer software in accordance with paragraph (e) below.
- (2) Recipient shall have the right to:
- (i) Use, release to others, reproduce, distribute, or publish any data first produced or specifically used by Recipient in the performance of the Project Agreement, except to the extent provided in paragraph (d) below or otherwise expressly set forth in this Project Agreement;
 - (ii) Protect from unauthorized disclosure and use, those data which are limited rights data or restricted computer software to the extent provided in paragraph (e) below; and
 - (iii) Establish claim to copyright subsisting in data first produced in the performance of this Project Agreement to the extent provided in paragraph (c) below.

(c) Copyright

- (1) In accordance with the STCU Statute, all rights worldwide to copyrights belong to Recipient. The Recipient and the Partner have agreed to protect and allocate such copyrights as specified in paragraph (c)(2) below.
- (2) The Recipient has title to copyrights in the New Independent States. The Recipient hereby grants to the Technical Monitor the entire right, title and interest to copyrights in all countries other than the New Independent States. Recipient acknowledges the right of the Technical Monitor to execute all documents necessary to register copyrights in said countries. Copyrighted works jointly created by Recipient and the Technical Monitor shall be jointly owned.
- (3) Recipient acknowledges that each of the Technical Monitor, the U.S. Government, Center, and each Party to this STCU Project Agreement has for itself and others acting on its behalf, a royalty-free, nonexclusive, irrevocable worldwide copyright license to reproduce, prepare derivative works, distribute copies to the public, and perform publicly and display publicly, by or on behalf of each of them, all copyrightable works produced in the performance of this Project Agreement.
- (4) For all copyrighted computer software produced in the performance of this Project Agreement, the party owning the copyright shall provide the source code, an expanded abstract, and the object code and the minimum support documentation needed by a competent user to understand and use the software to DOE's Energy Science and Technology Center, P.O. Box 1020, Oak Ridge, TN 37831. The U.S. Government shall have unlimited rights in said expanded abstract.

- (5) Recipient agrees to place copyright and other notices, as appropriate for the protection of copyright, in human-readable form onto all physical media, and in digitally encoded form in the header of machine readable information recorded on such media such that the notice will appear in human-readable form when the digital data are off-loaded or the data are accessed for display or printout.
 - (6) Recipient shall not, without prior written permission of the Partner, incorporate in data delivered under this Project Agreement any data not first produced in the performance of it and which contains a copyright notice, unless Recipient identifies such data and grants to the U.S. Government, or acquires on its behalf, a license of the same scope as set forth in paragraph (3) above, provided, however, that if such data are computer software, the U.S. Government shall acquire a copyright license as set forth in paragraph (e)(3) below if included in this Project Agreement or as otherwise may be provided in a collateral agreement incorporated in or made part of it.
- (d) Release, publication, and use of data
- (1) Recipient shall have the right to use, release to others, reproduce, distribute, or publish any data first produced or specifically used by Recipient in the performance of this Project Agreement, except to the extent such data may be subject to the U.S. federal export control or national security laws or regulations, or unless otherwise provided below in paragraph (d)(2) or expressly set forth in this Project Agreement.
 - (2) Recipient agrees that to the extent it receives or is given access to data necessary for the performance of this Project Agreement, which contain restrictive markings, Recipient shall treat the data in accordance with such markings unless otherwise specifically authorized in writing by Partner.
- (e) Protection of limited rights data and restricted computer software
- (1) When data are specified to be delivered under this Project Agreement and qualify as either limited rights data or restricted computer software, if Recipient desires to continue protection of such data, Recipient shall withhold such data and not furnish them to the Technical Monitor, Partner or Center under this Project Agreement except as provided for in paragraphs (2) and (3) below. As a condition to this withholding, Recipient shall identify the data being withheld and furnish form, fit, and function data in lieu thereof. Limited rights data that are formatted as a computer database for delivery to the Technical Monitor or Partner are to be treated as limited rights data and not restricted computer software.
 - (2) Limited Rights [This paragraph can be deleted if it is determined that there is no necessity for delivery of Limited Rights Data under this Project Agreement.]

Partner may require by written request the delivery of limited rights data that has been withheld or would otherwise be withholdable. If delivery of such data is so required, Recipient may affix the following legend to the data and the Technical Monitor and the U.S. Government will thereafter treat the data in accordance with such Notice:

LIMITED RIGHTS NOTICE

These data are submitted with limited rights under STCU Project Agreement No. _____. These data may be reproduced and used by or on behalf of the U.S. Government with the express limitation that they will not, without written permission of Recipient, be used for purposes of manufacture nor disclosed

outside the (insert name of the Technical Monitor) or the U.S. Government; except that (insert name of the Technical Monitor) or Government may disclose these data outside (insert name of the Technical Monitor) or the U.S. Government for use and evaluation by other contractors and/or entities participating in the Government's program of which this Project Agreement is a part provided that (insert name of the Technical Monitor) or the U.S. Government makes such disclosure subject to prohibition against further use and disclosure.

(END OF NOTICE)

- (3) Restricted Rights [This paragraph can be deleted if it is determined that there is no necessity for the delivery of Restricted Computer Software under the Project Agreement.]

The Project Agreement may identify and specify the delivery of restricted computer software, or Partner may require by written request the delivery of restricted computer software that has been withheld or would otherwise be withholdable. If delivery of such computer software is so required, Recipient may affix the following legend to the computer software and the Technical Monitor and the U.S. Government will thereafter treat the computer software in accordance with the Notice:

RESTRICTED RIGHTS NOTICE

- (1) This computer software is submitted with restricted rights under STCU Project Agreement No. _____. It may not be used, reproduced, or disclosed by the Technical Monitor or the U.S. Government except as otherwise expressly stated in this Project Agreement.
- (2) This computer software may be:
 - (a) Used or copied for use in or with the computer or computers for which it was acquired, including use at any Government installation to which such computer or computers may be transferred;
 - (b) Used or copied for use in a backup computer if any computer for which it was acquired is inoperative;
 - (c) Reproduced for safekeeping (archives) or backup purposes;
 - (d) Modified, adapted, or combined with other computer software, provided that the modified, combined, or adapted portions of the derivative software incorporating restricted computer software are made subject to the same restricted rights;
 - (e) Disclosed to and reproduced for use by any U.S. Government contractors in accordance with subparagraphs (2)(a) through (d) of this Notice, provided the DOE facility or the U.S. Government makes such disclosure or reproduction subject to these restricted rights; and
 - (f) Used or copied for use in or transferred to a replacement computer.
- (3) If this computer software is published copyrighted computer software, it is licensed to the U.S. Government without disclosure prohibitions, with the minimum rights set forth in paragraph (2) of this Notice.

- (4) This Notice shall be marked on any reproduction of this computer software, in whole or in part.
(END OF NOTICE)

(f) Royalty Sharing

To the extent that the Technical Monitor licenses to a third party any copyrighted work produced in the performance of this Agreement which results in income therefrom, Recipient and the Technical Monitor will share the net income therefrom fifty (50%) to Recipient and fifty percent (50%) to the Technical Monitor. Net income is gross income less any expenses and costs associated with the licensing and protection of the copyrighted work including, but not limited to, the costs of obtaining and maintaining the copyright. The Technical Monitor will provide Recipient annual reports setting forth the licensing activity for said copyrighted works by the Technical Monitor during the reporting period. The Technical Monitor will provide that any agreement to license a copyrighted work produced in the performance of this Agreement will be subject to the royalty sharing arrangement between the Technical Monitor and Recipient.

(g) Employee Agreements

Recipient shall obtain agreements to effectuate the provisions of this Rights in Data clause from all persons in its employ who perform any part of the work under this Project Agreement.

IV. ADDITIONAL DATA REQUIREMENTS [This clause can be deleted if all technical data requirements are known in advance of entering into the Project Agreement and are set forth in the Work Plan.]

- (a) In addition to the data (as defined in Clause III, Rights in Data-General) specified elsewhere in this Agreement to be delivered, Partner may, at any time during Agreement performance or within a period of three years after acceptance of all items to be delivered under this Project Agreement, order any data first produced or specifically used in the performance of this Project Agreement.
- (b) The Rights in Data-General clause included in this Agreement is applicable to all data ordered under this Additional Data Requirements clause. Nothing contained in this clause shall require Recipient to deliver any data the withholding of which is authorized by the Rights in Data-General clause of this Project Agreement, or data which are specifically identified in this Project Agreement as not subject to this clause.
- (c) When data are to be delivered under this clause, Recipient will be compensated for converting the data into the prescribed form, for reproduction, and for delivery.
- (d) Partner may release Recipient from the requirements of this clause for specifically identified data items at any time during the 3-year period set forth in paragraph (a) of this clause.

V. BACKGROUND INTELLECTUAL PROPERTY [This clause can be deleted if it is determined that no Recipient Background Intellectual Property is to be used during the performance of the Project Agreement.]

"Background Intellectual Property" is intellectual property (e.g., inventions, software, copyrights, trademarks) belonging to Recipient that was in existence before this Project Agreement. A background invention is an invention or discovery of the Recipient that was conceived outside of this Project Agreement and not first actually reduced to practice (i.e., demonstrated) under this Agreement. Recipient has identified the following Background Intellectual Property that may be used in the performance of this Project Agreement: