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C. Russia

Cheryl
Draft from
Jeff Cohen - Let's Discuss
- Paul

August 10, 2000

The Honorable Madeleine K. Albright
Secretary of State
The Department of State
2201 C Street, NW
Washington, D.C. 20520-7261

Dear Dr. Albright,

As a part of the United States' ongoing efforts to assist the former Soviet Republics in converting operations in the area of biological weapons to non-defense-related fields, we encourage bilateral US-Russian work in the area of HIV/AIDS prevention and in efforts to find a vaccine.

Multiple US programs are currently aimed at helping Russians convert physical facilities from Soviet defense operations to scientific laboratories and moving the scientists themselves from developing nuclear, biological and chemical weapons to valuable peacetime activities. These programs include the State Department's International Science and Technology Center in Moscow, the Pentagon's Defense Threat Reduction Agency, and the department of Energy's Nuclear Cities Initiative, Initiatives for Proliferation Prevention, and Materials, Protection, Control and Accountability program.

These programs are in the interest of American national security, and contribute to overall worldwide nonproliferation. Therefore, as a part of this spending, we would encourage conversion programs that employ Russian scientists in the worldwide effort to find a vaccine for AIDS. As you know, AIDS has reached epidemic proportions, and President Clinton recently declared the disease a threat to our national security.

Russian scientists already are working in the area of HIV/AIDS. Their research on finding a vaccine through the "Vaccine for a new Generation" program has received a small amount of funding from the Russian government since 1997. Another program, the Biotechnology Engagement Program" has received international support from the US.

In your interactions with the Russian government, we urge you to encourage further funding for these programs, and to assure Russian leaders that the U.S. stands ready to assist Russian scientists in this area. The race is on for a cure and a vaccine; when it comes to AIDS and HIV, we must pool our resources and employ the knowledge of the best scientists around the world.

Thank you for your attention to this serious matter.

Sincerely,

Ellen O. Tauscher
Member of Congress



BIOMEDICAL CENTER

7, Pudozhskaja St., St.Petersburg, Russia 197110 ☎: 7(812) 230-4872, 7(812) 230-4959, 7(812)230-7969

E-mail: biomed@mailbox.alkor.ru

10/01/99

St. Petersburg

Ms. Sandra L. Thurman
Director,
White House Office of National AIDS Policy

Dear Sandy,

I hope everything is going well in your Office. Last June we had a very productive meeting with Dr. Nathanson's group and the role of Todd in this success was very important. We in Russia are now at the very important point when correct decisions may significantly accelerate the collaboration of our countries in the field of HIV vaccine development. Russia is currently negotiating with the World Bank the considerable loan (\$ 150 mln) for AIDS and tuberculosis. Russian government suggests to forward part of the loan (\$55 mln) for the purpose of HIV vaccine development. This idea was supported by Dr. Nathanson's group. The WB delegation headed by Annette Dixon (health sector leader, Human Development Sector Leader, Europe and Central Asia Region) and Joana Mira Godinho (Public Health specialist, the same unit) are strongly opposing this. The situation seems strange to the Russian side because in June President of Russia has received a letter from the President of the World Bank encouraging Russia to develop HIV vaccine. As you know, last April World Bank had a meeting in Paris which recommended to develop the national HIV vaccine programs through the Adaptable Program Loan from the World Bank.

I urgently need some support in the World Bank. People who work with HIV vaccine program in the World Bank are Mr. Joseph E. Stiglitz, Senior Vice President, Development Economics and Chief Economist; Mr. Geoffrey Lamb, Acting Vice President, Resource Mobilization and Cofinancing and Co-chairs of WB AIDS vaccine task force Martha Ainsworth and Amie Batson.

Please, help.

Yours,

Andrei P. Kozlov, Ph.D.
Coordinator,
Russian HIV vaccine Problem

cc Mr. Todd Summers

P.S. During their visit to Russian Parliament members of the WB delegation were told that without vaccine component Russian Parliament will not approve the loan.

P.P.S. I have just talked to Amie. She told me that there could be some concerns in the WB about R&D nature of HIV vaccine project. This is not completely so, because considerable part of the project is devoted to creating the infrastructure for monkey trials and cohorts for Phase III trials. This will be not only for Russia, but for the World.

ONE HUNDRED SIXTY EIGHT

ONE HUNDRED SIXTY EIGHT

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JAMES E. OFFICIAN, CHIEF OF STAFF

U.S. House of Representatives
Committee on Commerce
Room 2125, Rayburn House Office Building
Washington, DC 20515-6115

December 21, 1999

Russia

RECEIVED
DEC 12 PM 3:53
U.S. HOUSE OF REPRESENTATIVES

Dr. Harold E. Varmus
Director
National Institutes of Health
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Dr. Varmus:

Pursuant to Rules X and XI of the U.S. House of Representatives, the Committee on Commerce is investigating the adequacy of security and controls to protect the National Institutes of Health's (NIH) research laboratories. In connection with this matter, the Committee is interested about certain aspects of foreign scientists working at the NIH laboratories.

To assist our inquiry, please provide the following information or related records by January 5, 2000:

- (1) Since the demise of the Soviet bloc, how many Russian national doctors or researchers have been used as consultants or collaborating researchers at NIH or its related laboratories?
- (2) How many Russian national doctors or researchers are at NIH currently carrying J-1 visas, or used as consultants or collaborating researchers at NIH or its related laboratories as of December 10, 1999? For each of these Russian doctors/researchers, identify by name, medical/scientific background, the type of research, their contribution to the research, the laboratory to which they are assigned and the biosafety level of the laboratory, and whether any financial stipends have been paid to these individuals. Have any of these individuals been assigned to the Biosafety Level 4 facilities at Fort Detrick, Maryland?
- (3) Have any of these doctors or researchers transferred organisms, vectors, or biohazardous materials to the United States as part of their NIH research? If so, please provide all import permits for the transferred materials.

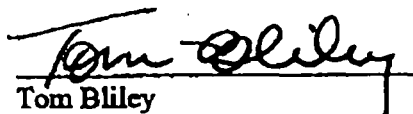
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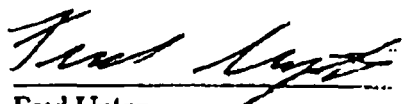
- (4) Are these doctors or researchers allowed to take the results of research at NIH with them when they return to Russia?
- (5) Have any of these doctors or researchers ever been used by the Russian military complex as researchers in the development of biological weapons?

Please note that, for the purpose of providing records relating to NIH research involving Russian scientists, the terms "records" and "relating" should be interpreted in accordance with the Attachment to this letter.

Thank you for your assistance. If you have any questions, please contact Alan Slobodin of the Committee staff at (202) 225-2927.

Sincerely,


Tom Bliley
Chairman


Fred Upton
Chairman
Subcommittee on Oversight and
Investigations

cc: The Honorable John D. Dingell, Ranking Member
The Honorable Ron Klink, Ranking Member
Subcommittee on Oversight and Investigations

Attachment

ATTACHMENT

1. The term "records" is to be construed in the broadest sense and shall mean any written or graphic material, however produced or reproduced, of any kind or description, consisting of the original and any non-identical copy (whether different from the original because of notes made on or attached to such copy or otherwise) and drafts and both sides thereof, whether printed or recorded electronically or magnetically or stored in any type of data bank, including, but not limited to, the following: correspondence, memoranda, records, summaries of personal conversations or interviews, minutes or records of meetings or conferences, opinions or reports of consultants, projections, statistical statements, drafts, contracts, agreements, purchase orders, invoices, confirmations, telegraphs, telexes, agendas, books, notes, pamphlets, periodicals, reports, studies, evaluations, opinions, logs, diaries, desk calendars, appointment books, tape recordings, video recordings, e-mails, voice mails, computer tapes, or other computer stored matter, magnetic tapes, microfilm, microfiche, punch cards, all other records kept by electronic, photographic, or mechanical means, charts, photographs, notebooks, drawings, plans, inter-office communications, intra-office and intra-departmental communications, transcripts, checks and canceled checks, bank statements, ledgers, books, records or statements of accounts, and papers and things similar to any of the foregoing, however denominated.
2. The terms "relating," "relate," or "regarding" as to any given subject means anything that constitutes, contains, embodies, identifies, deals with, or is in any manner whatsoever pertinent to that subject, including but not limited to records concerning the preparation of other records.



JAN 7 2000

National Institutes of Health
Bethesda, Maryland 20892

The Honorable Tom Bliley
Chairman
Committee on Commerce
House of Representatives
Washington, D.C. 20515

Dear Mr. Chairman:

As agreed with Committee staff, this will serve as an interim response to your letter of December 21, 1999, to Dr. Harold Varmus requesting information on Russian scientists at the National Institutes of Health (NIH). Additional information regarding our systems of security and safety will be provided by January 25.

- (1) Since the demise of the Soviet bloc, how many Russian national doctors or researchers have been used as consultants or collaborating researchers at NIH or its related laboratories?

Since the demise of the Soviet bloc in August 1991, there have been 411 Russian scientists at the NIH.

- (2) How many Russian national doctors or researchers are at NIH currently carrying J-1 visas, or used as consultants or collaborating researchers at NIH or its related laboratories as of December 10, 1999? For each of these Russian doctors/researchers, identify by name, medical/scientific background, the type of research, their contribution to the research, the laboratory to which they are assigned and the biosafety level of the laboratory, and whether any financial stipends have been paid to these individuals. Have any of these individuals been assigned to the Biosafety Level 4 facilities at Fort Detrick, Maryland?

There are currently 115 Russian scientists at the NIH. The enclosed list provides the name, medical/scientific background, and the Institute/Center and laboratory assigned. Of the 115, six are not receiving a financial stipend and these are noted on the enclosed list. The NIH has no Biosafety Level 4 facility at Fort Detrick. The remaining information will be provided by January 25.

- (3) Have any of these doctors or researchers transferred organisms, vectors, or biohazardous materials to the United States as part of their NIH research? If so, please provide all import permits for the transferred materials.

Information will be provided by January 25.

Page 2 - The Honorable Tom Bliley

- (4) Are these doctors or researchers allowed to take the results of research at NIH with them when they return to Russia?

NIH-supported researchers, including those in the NIH Visiting Program, work to publish their research findings in the open literature. Research notebooks, including information on experiments in progress or findings not yet suitable for publication, are the property of the U.S. government. It is not unusual for scientists to maintain a copy of their research material, however, that would be helpful to them to continue specific lines of research once they return home or to another institution outside of NIH.

- (5) Have any of these doctors or researchers ever been used by the Russian military complex as researchers in the development of biological weapons?

Information will be provided by January 25.

A similar letter has been sent to Congressman Fred Upton, Chairman of the Subcommittee on Oversight and Investigations.

Sincerely yours,

A handwritten signature in black ink, reading "Ruth L. Kirschstein". The signature is written in a cursive, flowing style.

Ruth L. Kirschstein, M.D.
Acting Director

Enclosure

2/13/00

Sandy - FYI

This is one
of the articles
Dr. Andrei Koslov refers to.
I will review + track down
the secansare as well.

Paul

The New York Times Magazine

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A Stalinist Antibiotic Alternative

A hoary Soviet method for fighting infections may prove invaluable in an age of antibiotic resistance. Maybe that's why pharmaceutical companies are flocking to a remote laboratory in Tbilisi. By LAWRENCE OSBORNE

In a barely heated ward for newborns on the top floor of the Georgian Republic Children's Hospital, Tamila Gogitidze carefully opens a glass ampul filled with amber liquid. The hospital, in the Degomi suburb of Georgia's decaying capital city, Tbilisi, is a spartan affair: its radiators are



High-tech it no longer is, but the Eliava Institute paved the way in phage research.
Photograph by Harf Zimmermann

ramshackle, the electricity intermittent and the raw concrete heavy on the eyes. A few American posters of babies cavorting in cabbages seem direly out of place. The liquid trapped inside the ampul, meanwhile, can be identified from a box on the floor. Its label is Latin: Bacteriophagum Intestinalis Fluidum. Gogitidze, a nurse on the intensive care unit for newborns, cracks open the ampul, pours the liquid onto a teaspoon and prepares to administer it to one of her babies, a 3-month-old boy abandoned at the hospital a few days before by his impoverished family. He is screaming lustily.

"Look," Gogitidze says, holding up a tiny wrist. "The parents made a kind of crude tattoo so that they can identify him later on. But for now, we must focus on his intestinal infection."

The fluidum is tipped like any cough syrup into the boy's blubbering mouth. His face contorts into a horrible wince; I look apprehensive. But Dr. Tamar Gotua, head of the intensive care unit, takes my arm and says: "We use them with almost all our children. Don't look so worried!"

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It's hard not to feel worried in Georgia. After years of bloody civil war following the collapse of the Soviet Union, the republic is in free fall. Electricity runs for only part of the day; blackouts are a daily, if not hourly, occurrence. Nevertheless, in this dilapidated neonatal ward a possibly revolutionary medicine, one essentially unknown in the West, is being casually administered on a simple teaspoon: bacteriophages, or microscopic viruses that actually "eat" bacteria.

Lawrence Osborne is the author of "Paris Dreambook." He last wrote for the magazine about Nicaraguan sign language.

Downstairs in the same hospital, I talk with Dr. Irakli Pavlenishvili, head of pediatrics, in an office so cold that our breath mists. The doctor offers me some Greek brandy and warms his hands by a portable electric heater. We chain-smoke furiously. "We've been using phages for years," he says briskly, looking up nervously at the flickering lights. "There are no major side effects. They're a living, natural force, not a toxic chemical. I wish our electricity were as reliable!"

Today, the West is paying renewed attention to this unheralded therapy created behind the Iron Curtain. The reason: antibiotic resistance. Although drugs like penicillin have held killer bacteria at bay for half a century, the bugs keep genetically adapting to them, evolving into tougher, smarter variants of ancient adversaries. The systematic overuse of antibiotics by doctors, especially in the United States, has helped breed "superbugs" -- bacteria resistant to even the most potent antibiotics, like vancomycin.

Last year, The New England Journal of Medicine published an alarming editorial about superbugs. "The outlook is rather grim," it wrote. "The adaptive potential of the microbial world is such that for each new antibiotic that is introduced, several escape mechanisms are soon devised."

Alexander Tomasz, a leading microbiologist at Rockefeller University, agrees: "The miracle days of antibiotics are over. We simply didn't think enough about the evolutionary consequences of drug use." With leading medical researchers in the West looking anxiously for antibiotic alternatives, bacteriophage therapy is suddenly looking "very promising," as Tomasz puts it.

"I'm convinced that bacteriophages will work," says Carl Merrill, chief of the biochemical genetics laboratory at the National Institutes of Health. "But there's the psychological obstacle of a new treatment coming from the former Soviet Union. It's unusual, to say the least."

They may sound exotic, but bacteriophages are in fact among the most common organisms on earth. (The word derives from the Greek *phagin*, "to eat.") Viral predators only one-fortieth the size of the average bacteria cell, they swarm unseen around us, busily searching and destroying their favorite food: germs. In electron microscope images, phages show up as ghostly, spiderlike creatures with transparent box-shaped heads, rigid tails and a tangle of legs for gripping their prey. They are so tiny that a single drop of

tap water may contain a billion of them.

How do phages kill bacteria? The answer is, with chilling efficiency. Latching onto the walls of a bacteria cell, the phage injects it with the genetic material stored in its very own head. Like a living syringe, it gradually empties itself into the victim and takes over its genetic machinery. Inside the helpless bacteria, bits and pieces of "daughter" phages begin to appear with sinister rapidity: rows of little heads, lines of tails, then legs. These different body parts assemble into miniphages, using the host cell as a kind of factory. As the phages multiply exponentially inside it, the bacterium's walls weaken -- then explode like a soap bubble. Scientists call this rather nightmarish process "lysis." It is the flash point of a gigantic microbial war between phages and bacteria, in which humans are a mere side issue.

'We've been using phages for years,' says one Tbilisi doctor, looking at the flickering lights. 'There are no major side effects. They're a living, natural force, not a toxic chemical. I wish our electricity were as reliable!'

These deadly microscopic hit men were discovered independently during World War I by the English microbiologist Frederick Twort and the flamboyant Canadian biologist Felix d'Herelle, then working in a laboratory at the Institut Pasteur in Paris. It was d'Herelle who gave them their name in a 1917 paper that predicted a revolution in the treatment of infectious diseases.

D'Herelle first discovered bacteriophages while working in the Mexican state of Yucatan in 1910. He noticed them in the most unlikely of places: the diarrhea of locusts. During an invasion of these insects, d'Herelle collected sick specimens and observed their abundant stools. He concluded that the locusts were suffering from septicemia caused by coccobacilli bacteria. D'Herelle smeared some of the diarrhea onto plates of agar to grow cultures, but then noticed something odd. After a while, clear circular spots a few millimeters across had appeared in the agar, suggesting that something was munching away at the coccobacilli. What were these tiny bacteria-eaters?

Back at the Institut Pasteur, d'Herelle repeated the experiment in 1915 with stools taken from a Paris-based squadron addled with dysentery. In the excrement of the officers, d'Herelle again detected agents that consumed the bacteria spontaneously. Nature, d'Herelle boldly announced to the world, had provided humankind with a living, natural weapon against germs.

Phages were popularized by Sinclair Lewis in his 1925 novel "Arrowsmith," about a young doctor who goes to the West Indies to use them against an epidemic of bubonic plague. "You may," says one of the novel's characters to Martin Arrowsmith, who was inspired by the real-life d'Herelle, "have hit on the supreme way to kill pathogenic bacteria!"

But it was not to be. Phages proved to be a hit-or-miss affair as a therapy. One problem was that there are hundreds of types of

phages, and each type kills only one variety of bacteria. Predator and prey must be perfectly matched, a daunting process. What's more, there were early problems with purification. When phages burst out of the victim's cell, they leave behind debris that can contaminate the solution. This debris can prove fatal to humans, a problem that the purification technologies of the early days were unable to solve.

As a result of these difficulties, phages were quickly outpaced by a rival drug: penicillin. Although Eli Lilly actually manufactured therapeutic phages for the United States market in the 1930's, after World War II they were largely consigned to the margins of Western medicine -- even as they took center stage in DNA research, where their simple molecular structure made them an ideal tool for peering



The Eliava lab where Nina Chanishvili, Thea Gionti, Maya Merabishvili and Tamar Giorkhelidz work is unheated. Photograph by Harf Zimmermann

into the inner workings of genes. Sir Francis Crick and Max Delbruck, two architects of DNA theory, were phage researchers. Phage research helped unlock molecular biology at the very moment that they disappeared from the medical scene.

Yet there is a twist to this story. The aristocratic d'Herelle was a passionate Communist and admirer of Stalin. In 1934, he accepted an invitation from the Soviet government to join the Institute of Bacteriology in Tbilisi, recently set up by a young Georgian microbiologist named George Eliava. The Eliava Institute, as it became known, became the world's leading center of therapeutic phage research. One of its first successes was a powerful dysentery phage for the Red Army during the World War II. Over the ensuing decades, the institute began supplying precisely targeted phages to hospitals all over the Soviet bloc. The Eliava Institute became the largest phage library in the world, with a permanent "museum" of more than 300 phage clones.

"We've been perfecting bacteriophages as a medicine for over 70 years, just as d'Herelle said we could," explains Nina Chanishvili, a senior researcher at the Eliava Institute today. "But has anyone been listening?"

On an icy December day, Chanishvili and I walk through the hilly Tbilisi district of Saburtalo on our way down to the Eliava Institute. The path winds vertiginously through plots of spindly pomegranate trees touched with snow. Clumped along the hillside are rotting Soviet-era apartment blocks. On the streets, the shops are lighted only with candles.

Nina's uncle, Teimuraz Chanishvili, has helped direct the Eliava Institute for a quarter of a century, and she, too, has devoted most of her life to phage research. But the last 10 years have been cruel. In recent years, she says, the institute's phage output has dwindled

alarmingly. Virtually unpaid, the institute's workers now cling to a fading infrastructure. When high-tech equipment breaks down, they must work with improvised materials. Also, adds Chanishvili, "because of the power cuts, we've lost about half of our phage library." (Phage cultures must be refrigerated.) Georgia's economic collapse has dwindled the demand for phages as well. Once the institute manufactured phage sprays, salves, ointments, tablets -- you name it. But now, even at \$3 to \$5 for a box of 10 ampuls, many of Tbilisi's sick simply cannot afford them.

The institute, however, still sits in its graceful park of cypresses overlooking the Mtkvari River, and over the wall I see the handsome cottage that Stalin had specially built for d'Herelle. It is still called "d'Herelle's cottage," though it was later occupied by the Georgian K.G.B. Inside, the institute is a cavelike labyrinth of damp cement corridors, stairwells dripping wires and mournfully antiquated labs. The old fermentation vats that used to churn out phage preparations for the Soviet Ministry of Health stand abandoned in a room with no glass in the windows.

Upstairs, Chanishvili shares a cramped and unheated lab with a fellow researcher, Marina Tediashvili, and half a dozen young medical students. They are all women. They are all shivering. "Of course," says Tediashvili, "the men naturally move on to better things." Equipment is largely rudimentary. Among the centrifuges, water baths and piles of petri dishes stand dozens of beer and vodka bottles that the women use as containers for their solid agar. To melt the agar, they pop one of the vodka bottles inside an old Nescafe tin sitting on a hot plate. "We like vodka bottles," Chanishvili feels obliged to explain, "because they're so transparent."

The interns spend most of their time on the tedious chore of planting phage cultures in the specimens of bacteria, turning each petri dish into a kind of phage farm. I watch as one of the women sterilizes the tip of an applicator in a Bunsen burner, drips a blob of phage solution onto a plate of *E. coli* and carefully closes the plastic lid. "*E. coli* causes epidemics worldwide," explains Tediashvili. "But these phages find *E. coli* tasty. They go through it like Oreos."

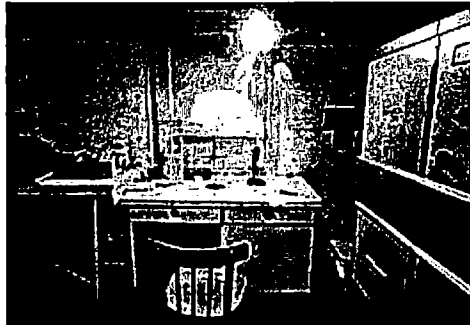
Holding up an *E. coli* dish that has been incubated for two days, she points to a smattering of irregular, clear circles carved out of the agar. They look like the perforations of a shotgun blast. "Isn't that beautiful?" she whispers. A dish of salmonella is peppered with smaller, more regular bullet holes.

Chanishvili explains that she and her colleagues initially catch phages in gunky places where the creatures are known to thrive: sewage water, for example. They are then stored in a liquid broth kept in a refrigerator at 4 degrees Celsius. Oddly enough, they don't need to be fed with tasty germs to stay alive. "Phages can live for months without food," Chanishvili says. "Without additional germs to feed on, they cannot multiply out of control." If their numbers begin to decrease, however, a few bugs are thrown to them and they multiply again.

In the same wing, I am taken to see Amiran Meipariani, head of phage research. Meipariani has been here since 1946, at the height

of the Stalin era, and his sardonic blue eyes seem to have seen it all. Like most Georgian doctors, he chain-smokes and shrugs frequently. His office is filled with disconnected Soviet telephones; on the wall hangs a faded portrait of Felix d'Herelle.

"As you can see, we've fallen on hard times," he says, shrugging. "But it is now realized worldwide that an alternative to antibiotics should be sought and that the best one is bacteriophages. Perhaps it's a boon for us. Did you know that NATO is now interested in one of our inventions?" His eyes light up puckishly. He is referring to a topical phage application invented by the Eliava



"As you can see, we've fallen on hard times," says Eliava's head of phage research.

Photograph by Harf Zimmermann

Institute and known as a "PhageBioDerm," a kind of bandage saturated with a cocktail of five to nine different phages that can treat infected burn wounds. It is the perfect military Band-Aid. Russian soldiers have used them in Chechnya. "Of course, women and kids can use them in the kitchen, too," he adds with a sales-pitch smile.

The Eliava has a local patent on the phagoderm, which it manufactures itself along with the "intestiphage," the 17-phage cocktail I saw being administered to the abandoned baby. All in all, the Eliava produces about 10 different phage applications that target about 15 different bacteria genera. By creating drugs that combine many phages at once, their administration can be simplified to a single dose.

Considering the difficulties involved in doing science in Georgia, the advancements made by the Eliava are remarkable. Chief among these has been the creation of an intravenous remedy to the deadly staph aureus bacteria, a strain that threatens to one day outpace vancomycin. According to the Eliava, it's been used successfully on dozens of patients.

In the past few years, the Eliava's skill has attracted the attention of Western entrepreneurs eager to harness the knowledge bottled up in Tbilisi's laboratories. But the Georgian scientists worry about this development as much as they celebrate it. Who will ultimately benefit from the commercial exploitation of their work? Will the Americans and Europeans simply steal their expertise and innovations? "The local market has collapsed," says Meiparinai with a final shrug. "But who will patent phages in the West? Who's going to make the millions?" Then he corrects himself. "The billions, I mean." Indeed, the worldwide antibacterials market is estimated to be worth \$25 billion a year.

So far, the Eliava's experience of cooperation with American companies interested in phages has not exactly been propitious. In 1996, a Canadian venture capitalist named Caisey Harlinton came to Tbilisi, eager to talk to the Chanishvilis about their work. What

happened next was, as Chanishvili puts it tersely, a "culture clash." Although a start-up company that came to be named Phage Therapeutics was quickly set up in Seattle, the planned Tbilisi affiliate was closed almost as soon as it opened. "Harlingten told me," says Chanishvili bitterly, "that the American consumer would never accept a medical product from the Soviet Union." Meanwhile, Phage Therapeutics is busy readying Eliava-inspired medicines for the U.S. market.

"We gave the Americans access to all this background research," she goes on, "and they simply walked away with it. They told us we were stupid at business. Well, that at least was true."

That evening, I meet with Teimuraz Chanishvili at his home on Kazbegi Street, a lampless street of elegant 19th-century Russian houses. A Nabokovian charmer now in his 70's, he greets me at the top of the stairs in his dressing gown. "Come and look at the TV," he says excitedly. "The Americans have stolen my phage photographs!" By one of those coincidences that even a journalist couldn't invent, there indeed is an American documentary about phages playing on the TV. Teimuraz's uncopyrighted images of phages float like extraterrestrial prawns across the screen. "I didn't get a cent!" he cries, shaking his finger at the screen.

Later, we have a calmer chat over chestnut soda, and he tells me the sad story of George Eliava. The man who established the bacteriophage's central place in Soviet medicine was not exactly rewarded for his efforts. When not doing brilliant science, Eliava was a handsome playboy who had the misfortune to fall in love with a woman also admired by Lavrenti Beria, Stalin's secret police chief. Despite Stalin's high regard for bacteriophages, it was Eliava's death warrant.

"Beria had Eliava shot in 1937 on a pretext," Teimuraz says matter-of-factly. "That's the way it was back then." He adds with a chuckle, "Thankless work, bacteriophages!"

As if on cue, the lights go out.

In the well-lighted laboratories in Europe and the United States, however, the prospects for phages are glittering. In this country alone, at least three start-up companies are vying to be the first to push a phage therapy through Food and Drug Administration approval. In addition to Harlingten's Phage Therapeutics in Seattle, there are Intralytix in Baltimore -- a company with numerous Georgian expats on the payroll -- and Exponential Biotherapies on Long Island, a small biotech company run by Dr. Richard Carlton that expects to petition the F.D.A. to begin clinical trials on a phage drug this spring.

Big challenges face these companies. One pitfall of early phage therapy was that wild phages are expelled very quickly by the body's filtering system, often reducing their effectiveness. The immune system, in other words, treats them as foreign bodies. Can new technologies, however, pinpoint "domesticated" phages that can linger longer in the body? While the Eliava has had some success on this front, American scientists hope to do even better.

The work of Carl Merrill has led the way. In the April 1996 edition of Proceedings of the National Academy of Sciences, the N.I.H. researcher published the result of some intriguing experiments with phages and mice. Essentially, he was able to selectively breed "mutant" phages that remained in the mice far longer than the wild variety. "We altered the code proteins in the phages," Merrill explains, "to make them more durable." In the same issue, the Nobel laureate Joshua Lederberg of Rockefeller University wrote, "This is an ingenious surmounting of one of the hurdles to the use of phage in therapy."

It was Merrill, recalls Carlton of Exponential Biotherapies, "who told me that phages had been used as a therapy back in the 30's. What sometimes limited them, though, was this problem of making them stick around inside your body. But today, with genetic engineering, we can selectively breed phages that can last thousands of times longer." This represents a huge advance. After all, a single phage can produce 40,000 daughters in an hour; one hour later, the number increases exponentially to 4 billion. As Carlton puts it, "It's the only drug that makes more of itself as it's actually being used!" In recent experiments with mice infected with the E. coli bacteria, Merrill reports, he cured every single animal with these long-life phages.

At University of Maryland labs used by Intralytix, Zemphira Alavidze, who also runs her own lab at the Eliava Institute, presides over the same array of petri dishes, jars of agar and phage phials. But the difference between Baltimore and Tbilisi is twofold. "Here," she says, "we have lots of mice to experiment on. And we can purify phage solutions using chromatography. Purification is much more tricky in Tbilisi -- and mice are just out of the question."

Purification and in-depth animal testing are essential first steps toward commercializing phages in the painstaking medical culture of the West. Clinical trials involving human patients are yet to come. On this front, the Georgians are way ahead of the Americans. Indeed, the Soviet bloc's headlong experiment with human patients may well turn out to be the greatest contribution of the embattled Tbilisi doctors to the eventual medical use of phages.

'I'm convinced that bacteriophages will work,' says Carl Merrill of the N.I.H. 'But there's the psychological obstacle of a new treatment coming from the former Soviet Union.'

Dr. David Shrayer, now a cancer researcher at Brown University, worked as a medical officer on the construction of the Baikal-Amur railroad in Siberia in the 1970's, where he says he regularly administered bacteriophages to Soviet construction workers. "Even back then," Shrayer says, "these Siberian workers were suffering from infections that were resistant to antibiotics. The phages worked splendidly. But here's the catch. D'Herelle and then the Soviets ruined the image of phages in the West by testing them on people without first conducting proper animal tests. Animal tests were expensive; patients were cheap. That was the tragedy of phages in the East. But it was also their trump card. We learned

that they really work."

The most exclusive private clinic in Tbilisi is the plastic surgery unit within the Clinical Diagnostic Center, a stone's throw from the university. The contrast with the children's hospital couldn't be greater. A small vestibule sports a soothing green fish tank, while Tchaikovsky burbles on the sound system. Open just a year, the clinic serves the liposuction needs of Tbilisi's rich. Here I sit with the elegant Dr. Iva Kuzanov, Georgia's top plastic surgeon, looking at an album of post-op photographs. They are stomach-turning.

"This man was bitten in the nose by a pit bull. See how handsome he is now? This woman came to us from San Francisco for a sex-change operation. What do you think of her penis?"

"Marvelous," I say.

There is an alarm clock hanging from it. "To prove the strength," Kuzanov says with a totally straight face. "We amputated her finger and put it inside. Amazing, no?"

What is really remarkable about the clinic, however, is the frequency with which phages are used to counter surgical-wound infections in these complex (if bizarre) cosmetic operations. Many of Kuzanov's patients are from the West, he says. "They come because of the low prices here." As for phages, Kuzanov claims, they've proved to be excellent for burn traumas or infections arising from accidents. He holds up a picture of a breast-reduction job. "We treated her lesions with phages. Look, a perfect recovery."

To see one of these phage patients for myself, however, I decide to call on the first person ever to have been treated with intravenous phages. His name is Prince Avtandil Chkheidze, M.D. He is a prince *and* a doctor. Chkheidze receives me in an imposingly austere office at his private clinic. Although it is freezing cold, he wears only a snappy maroon blazer. After first showing me a copy of his family's coat of arms, he hands me a more welcome glass of steaming Turkish coffee. "So you want to hear about phages?" he whispers like a character out of Edgar Allen Poe.

Chkheidze spins out his story. After graduating in 1976 from a Tbilisi medical school, he was posted to a gynecology clinic in Leningrad. Overworked and exhausted, he eventually fell ill with a severe lung infection. In time, he came to be additionally afflicted with a long-term purulent skin infection. Even though his hospital placed him in a top Soviet clinic with state-of-the-art Western medicine, its antibiotics made no difference. His skin infection worsened, and he begged to be allowed to return to Tbilisi. Once there, he asked his father, one of the city's leading doctors, to see if he could be treated with intravenous phages -- a procedure never carried out before. The risks were great. But unable to move and now dependent on crutches, Chkheidze didn't much care.

"At first," he says, "my father was horrified by my proposal. Then Teimuraz Chanishvili told us he had a staph aureus phage already tested on animals. But he was afraid to use it on humans."

They therefore had to find someone willing to administer the phages. In the end, Dr. Vakhtang Bochozishvili, a famous professor at the Sepsis Center in Tbilisi, agreed to do so. "It was a bit of a conspiracy," Chkheidze says. "I was the ultimate guinea pig."

On the fifth day of treatment, the prince threw away his crutches and went to a late-night party with his friends. The taboo on intravenous phages, he notes, was shattered with one blow. "On the seventh day I was completely cured. It was quite miraculous."

The possible implications of this strange fragment of medical history are enormous. Chkheidze says that he would like to introduce widespread intravenous phages into his clinic. In fact, he claims, his clinic doesn't use antibiotics at all to treat infection. He also claims that during the last 10 years of the Soviet system, approximately 20,000 people were cured of chronic sepsis by phages, though it is hard to verify such statistics. As it is, he adds: "I use them every day in my practice. They are excellent for pregnant women, extremely safe." He lowers his voice. "I use them in vaginal suppository form. They are pure gold."

But what of human patients in the West? This is a far more shadowy affair, since phages can be used only in extreme cases in which a dying patient's family gives explicit permission for their use. So far, such cases have been extremely rare. Last year, Nina Chanishvili was contacted by two Belgian brothers who had read about phage therapy on the Internet. Their 23-year-old sister lay dying of a severe post-measles viral infection of the brain. A trepanation in her skull to inject antibiotics, the brothers explained, had become infected with staphylococcus aureus. Could Chanishvili treat the secondary infection with phages?

"I just had to go," she says. "I brought the phages myself." According to Chanishvili, the secondary staph infection cleared up within days, though the girl remained mortally ill from her untreatable primary condition.

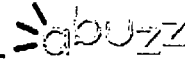
In another recent case, a woman dying of a Marfan-related heart problem in Toronto was treated for a staph infection by having a solution of phages sprayed directly onto her aorta. The infection was vanquished within 20 hours. (Two months later, the woman died of her heart condition.) Phage Technologies, which provided the medicine, hyperbolically hailed it as "the first use of phage therapy in the West in modern times."

Of course, one patient is far from the rigorous proof Western medicine requires; perhaps the staph infection would have cleared up on its own. Nevertheless, says Elizabeth Kutter, a leading American phage researcher at Evergreen State College in Olympia, "what this shows is that phages are ready to be used in the West."

The next international phage conference will be held this June in Montreal, d'Herelle's birthplace. It is difficult not to imagine the old Communist iconoclast smiling in his grave -- not to mention Comrade Stalin. "It's strange to think," says Nina Chanishvili, "that Stalin might be considered a medical benefactor of the 21st century!"

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February 06, 2000

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May 29, 2000

NOTE TO SANDY THURMAN FROM PETER HARTSOCK

Re: Attached Message from Russia

Dear Sandy:

Andrei Kozlov requested that I hand deliver the attached documents to you. We worked late into the night just before I left St. Petersburg to prepare these documents for you.

Please note the resolution which was passed last week in St. Petersburg which recognizes the causal relationship of HIV to AIDS. The passage of the resolution was witnessed by International AIDS Society President Elect Dr. Stefano Vella, who flew directly from Durban, South Africa to St. Petersburg, Russia to be present for the resolution's passage. I was there, too and I truly wish you could have been. It was absolutely magical and you were referred to with great love and respect.

This resolution is highly important because it is the product of independent Russian research which is not beholden to the U.S. or any other country. Thus, it provides you, the White House, and the U.S. with maximum support in dealing with the HIV-AIDS "controversy." Something else--because Russia and the Soviet Union were supportive of the African National Congress (ANC) for many years, Russia enjoys special credibility with the current South African regime. Remember that Andrei will be at Durban and is ready, willing, and able to assist you.

One last thing--Andrei requested that you mention to the President that Vladimir Putin is very supportive of cooperation in AIDS, including the HIV vaccine. In this time of uncertainty, such cooperation is particularly positive for both the U.S. and Russia and it is something on which the leaders of both countries can find common ground and point to with pride. Andrei said that any reinforcement for the cooperative U.S.-Russian AIDS efforts and HIV vaccine work at the upcoming Clinton-Putin meetings will greatly accelerate these positive efforts.

As Dickens said in *A Tale of Two Cities*, "It was the best of times; it was the worst of times." You are playing a special and vital role in contending with the worst and manifesting the best in this troubled but portentous time. In this respect, I can guarantee that you were with us in a spirit so wonderful and tangible that it was almost physical.

Best wishes and I hope you are well.

BIOMEDICAL CENTER

7, Pudozhskaja st., St.Petersburg, Russia 197110; Fax: 7(812) 230-4959; Phone: 7(812) 230-4872
E-mail: biomed@mailbox.alkor.ru

Ms. Sandra Thurman, Director
White House Office on National AIDS Policy
Washington, D.C.

Dear Ms. Thurman:

We are sorry that you were unable to be with us this past week at the 8th International Conference on AIDS, Cancer, and Related Problems in St. Petersburg.

Nonetheless, there were a number of successful outcomes, the most important of which is the attached resolution which was passed unanimously by the Russian Association Against AIDS (RAAA) and reaffirms Russian science's conclusion of the causal relationship of HIV and AIDS.

The passage of this resolution was witnessed by Dr. Stefano Vella, President Elect of the International AIDS Society and flew to St. Petersburg from Durban, South Africa to be with us at this historic event. The passage of the resolution was also witnessed by other international authorities on AIDS, including Dr. Peter Hartsock, of the U.S. National Institutes of Health. I have asked Dr. Hartsock to hand deliver to you our attached resolution on HIV/AIDS.

Most importantly, this resolution was passed based on rigorous Russian research and was a conclusion reached independently by Russia. The independence of the conclusion makes it all the more powerful and compelling and we hope that it will be of use to you in your endeavors. Russian and American scientists have independently reached their own conclusions but these conclusions coincide and thus confirm each other. Thus, the strong science of our two great countries unite us as equal partners in the spirit of Abraham Lincoln's immortal words, "United we stand; divided we fall."

Many best wishes to you in your noble work.

Sincerely,



Dr. Andrei P. Kozlov, Chairman of the Conference
Executive Director, Russian Association Against AIDS
Coordinator, Russian HIV Vaccine Program
Director, Biomedical Research Center

**8th INTERNATIONAL CONFERENCE “AIDS, CANCER
AND RELATED PROBLEMS”
MAY 19-24, 2000, ST. PETERSBURG, RUSSIA**

7, Pudozhskaja st., St.Petersburg, Russia 197110; Fax: 7(812) 230-4959; Phone:
7(812) 230-4872 E-mail: biomed@mailbox.alkor.ru

On the Occasion Of The 8th International Conference On AIDS, Cancer,
and Related Problems, Be It Resolved:

That the leading HIVAIDS researchers in Russia and the former Soviet Union do unanimously and solemnly declare that our rigorous scientific investigations, carried out for many years, demonstrate conclusively the strong causal relationship of the Human Immune Deficiency Virus (HIV) to Acquired Immune Deficiency Syndrome (AIDS).

Furthermore, claims to the contrary which have been discredited for many years, serve no useful purpose and, indeed, cause much needless sickness and death and should be considered genocidal because they undermine all HIV/AIDS prevention and treatment interventions.

Overwhelming scientific evidence, coming from many countries but all confirming the HIV/AIDS relationship, should be given maximum credence by the world scientific and public health community.



Dr. Andrei P. Kozlov, Chairman of the Conference
Executive Director, Russian Association Against AIDS
Coordinator, Russian HIV Vaccine Program
Director, Biomedical Research Center

St. Petersburg, Russia
May 23, 2000

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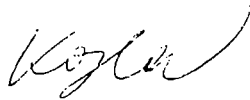
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Executive Director, Russian Association Against AIDS
Coordinator, Russian HIV Vaccine Program
Director, Biomedical Research Center

St. Petersburg, Russia
May 23, 2000

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Short Program

8th International Conference "AIDS, Cancer and Related Problems"

St. Petersburg, Russia (May 19–24, 2000)

House of Friendship, 21 Fontanka Embankment

19.05 Friday	15.00-17.00	OPENING CEREMONY (White-column Hall) Presentation of awards for outstanding contribution to campaign against HIV/AIDS Lectures of the award recipients		
	17.00	OPENING OF THE EXHIBITION (Knights' Hall)		
	17.15-18.00	PRESS-CONFERENCE (Conference Hall)		
	18.00	Banquet		
20.05 Saturday		<i>Conference Hall</i>		<i>Red Hall</i>
	9.00-10.00	TB WORKSHOP		
	10.00-11.00	Lecture of Academician R. V. Petrov, Vice-President of the Russian Academy of Science		
	11.00-13.00	Session 1: HIV Vaccine	TB WORKSHOP	
	14.00-17.00	Session 1: HIV Vaccine	Session 2: Human Oncoviruses	
21.05 Sunday	9.30-13.00	Session 3: Epidemiology of HIV Infection	Session 4: Cytokines in AIDS, Malignancy and Other Diseases	
	14.00-17.00	Session 5: Laboratory Diagnostics, Monitoring of HIV and Opportunistic Infections Round Table: "How many laboratory testing do we need for HIV, STDs and other infectious diseases?"	Session 6: Molecular and Fundamental Aspects of Tumor Growth	
22.05 Monday	9.30-13.00	Session 7: Molecular and Cellular Biology of HIV Infection	Session 8: HIV Infection Among IDUs and Possibilities of Its Prevention	
	14.00-17.00	Session 9: Experimental and Theoretical Biology	Session 8: HIV Infection Among IDUs and Possibilities of Its Prevention	
23.05 Tuesday		<i>Conference Hall</i>	<i>Red Hall</i>	<i>Golden Hall</i>
	9.30-13.00	Session 10: Biosocial aspects of HIV/AIDS	Round table: "Role of mass media in fighting against HIV epidemic"	Session 11: Epidemiology and Prevention of STDs
		<i>Conference Hall</i>		<i>Red Hall</i>
	14.00-17.00	NIMH Symposium: "Prevention of HIV infection"		Session 12: Molecular and Cellular Aspects of Stress Biology
	17.00	Meeting of the Association against HIV/AIDS		
24.05 Wednesday	9.30-13.00	International AIDS Society (IAS) Workshop on HAART		Session 13: Biotechnology Session 14: New Technologies
	14.00-17.00	Session 15: Pathogenesis and Clinical Problems of HIV/AIDS and Cancer		Session 16: Molecular Design, Directed Synthesis and Manufacturing of Substances and Drugs Against HIV/AIDS

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**Русский
журнал
ВИЧ/СПИД
и родственные проблемы**

Т. 3, № 2

**Russian Journal
of HIV / AIDS
and Related Problems**

**1999
Санкт-Петербург**

THE WHITE HOUSE
WASHINGTON

This is purportedly a letter from
The World Bank to the Russian
government supporting use of
a portion of a pending loan for
HIV vaccine research.

Idid

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Series:

Subseries:

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Language: Russian

Folder Title Russia [1]

OA/ID: 21064

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Document Title in cyrillic, purportedly from World Bank to GOR re
AIDS vaccine

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E-mail: biomed@mailbox.alkor.ru

29 June, 1999

Fax :

To: Mr. Todd Summers

From: Dr. Andrei Kozlov

Dear Todd,

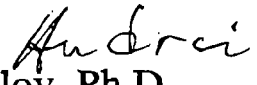
May I thank you for coming to St. Petersburg and for your most important impact for the success of our meeting. HIV/AIDS problem has substantial political aspect, and your comments on this issue during the meeting, in the Parliament and in the Ministry of Science were both deep and original.

My friends, scientists and politicians, have appreciated your participation very high.

I am faxing you the copy of the letter from the President of the World Bank to the President of Russia. As you can see, Russian President have further forwarded the letter to the Ministry of Foreign Affairs (Ivanov), Ministry of Economy (Shapovaliants), Ministry of Health (Starodubov) and Ministry of Finance (Kasjanov).

After my report to the Science Minister, Professor Kirpichnikov, on this matter he has also requested this letter from the Administration of the President. Ministry of Economy, in accordance with the deal with the Ministry of Foreign Affairs, will be responsible for work on this letter. I am currently involved in this work.

Please extend by best regards to Sandy and Sarah.

Yours,

Andrei P. Kozlov, Ph.D.
Coordinator,
Russian HIV Vaccine Project

An application for a credit from the International Bank for Reconstruction and Development

Summary

1.1. Project title

DEVELOPMENT OF AN AFFORDABLE HIV VACCINE AND A STRATEGY FOR ITS OPTIMAL USE

1.2. Project nature

The objectives of the project are to develop an effective and inexpensive HIV vaccine and to work out a strategy for optimal use of such vaccine to perform vaccination in Russian Federation. The attainment of said objectives implies the fulfillment of the following tasks:

- to determine what serotypes and subtypes of HIV-1 are circulating in Russia and what is their prevalence in different groups of HIV-infected people;
- to design different versions of HIV vaccine;
- to study, using animal models, the immune responses evoked by the vaccines and their protective effects;
- to conduct preclinical trials of candidate vaccines and to choose the most promising ones;
- to manufacture experimental vaccine batches sufficient for conducting clinical trials;
- to conduct clinical trials of a vaccine of choice;
- to develop the technology of the large-scale HIV vaccine production;
- to construct industrial facilities for HIV vaccine production;
- to develop, basing on the interdisciplinary approach, a strategy for the optimal use of HIV vaccine to perform vaccination in Russian Federation;
- to produce vaccine in an amount sufficient to vaccinate populations under the greatest risk of HIV-infection.

1.3. Cost

Total cost: US\$ 160 million.

The cost of the first stage (years 2000-2004): US\$ 55 million

1.4. Implementation period

Fifteen years.

1.5. Financial backing

The project will be implemented in three stages, each being 5 years long.

The project in its totality is meant to be backed primarily by a loan provided by IBRD and amounting to US\$ 152 million, which makes 95% of the total cost of the project.

Federal budget of Russian Federation will provide US\$ 8 million, which makes 5% of the total cost of the project.

Implementation of the first stage of the project (years 2000-2004) requires US\$ 55 million, of which US\$ 52 million are expected to come from IBRD and US\$ 3 million, from Federal budget of Russian federation.

Currently, the activities of the participants of the project engaged in the scientific part of HIV vaccine development are backed by RF Federal Budget, as far as it finances Russian Program “New Generation Vaccines and Diagnostic Systems of the Future” which includes a sector entitled “Anti-HIV/AIDS Immunizing Agents and Vaccines”. However, the funds allocated by this program are insufficient to develop HIV vaccine within shortest terms possible. Moreover, the program does not provision financial backing needed to manufacture experimental HIV vaccine batches for clinical trials, to design and build facilities for a large-scale HIV vaccine production, and to develop the strategy of its use.

1.6. Recoupment terms

Within twelve years after starting the large-scale HIV vaccine production.

1.7. Independent state expert appraisal

There exist positive expert judgments from State Scientific Center Institute of Immunology, RAMN Academician Prof. A.A. Vorobiyev, and Prof. K.P. Hanson, Director of Central Radio-Roentgenological Institute.

2. General information about the project

2.1. Objectives

The objectives of the project are defined by the following:

Human immunodeficiency virus (HIV) is an infectious agent which causes a disease with the mean asymptomatic period lasting for ten years, on average, during which an HIV-infected person can transmit the infection either sexually or via blood (blood transfusion, mother to child transmission, syringe sharing by drug users, etc.). At present, there are still no means to clear the human organism of the virus and to prevent the progression of the infection to its terminal stage, AIDS, which results in the premature death of infected subjects.

Starting from the mid-nineties, a dramatic increase in HIV infection incidence has been being observed in Russian Federation. In 1987, only 23 cases of HIV infection were registered in USSR. In 1998, there were 80 such cases. In 1995, 1061 cases were registered in Russia alone. In 1996, the number of cases reached 2556. According to the Ministry of Health of Russian Federation, by June 1998, the number of registered HIV-infected subjects in Russia was 8313, of which 317 subjects (110 children included) developed AIDS and 209 subjects (72 children) died of AIDS. The greatest number of HIV-infected subjects (2075) were registered in Kaliningrad followed by Krasnodar (1269), Rostov-on-Don (897), Moscow (823), Nizhniy Novgorod (549), Tver' (746), Saratov (341), St. Petersburg (195), and Tiumen' (150). These are the data about detected and registered cases of HIV infection. Actual numbers are likely to be significantly greater. The estimate of UNAIDS for Russian Federation is 40 000 cases by the end of 1998.

Before the explosive rise of HIV infection incidence, the main route of HIV spread was the sexual transmission. At present, the major portion of infected population is constituted by intravenous drug users (IDU). In the nearest neighbor countries, the sharp increase of HIV infection incidence is also observed among IDU. In Belorussia, 113 cases of HIV infection were detected in 1987 - 1995. During 1996, this number increased tenfold. By 1998, the number of registered cases of HIV infection was 1787, of which 94% were detected during the last two years. In Ukraine, in Nikolayevsk region alone, which, along with Odessa and Donetsk, is one of the main foci of HIV infection in this country, there are currently 3103 registered HIV-infected subjects, whereas only single cases were detected before 1994. On the whole, 14000 HIV-infected subjects have been registered in Ukraine by December 1997, and the estimate of the total number is 25000. All around the region the leakage of HIV from the IDU group by heterosexual transmission is observed and cases of mother-to-infant transmission are registered.

Thus, at present Russian Federation and its nearest neighbor states are going through the stage of HIV/AIDS epidemic that several years ago has been gone through by such countries as Thailand and India where, by now, millions of people are infected by HIV. It is important, in this respect, that social and economic conditions of Russia provide all factors known to promote HIV spread.

Still earlier, this stage of HIV spread was experienced by USA and Western Europe where first cases of the infection were found in early eighties. Since then, the numbers of HIV-infected subjects

in these regions reached 860 000 and 530 000, respectively. Global HIV estimates for the end of 1997, according to UNAIDS Annual Report, are 30.6 million infected people and 5.8 million new infections annually. The number of HIV-infected people increases by 16 000 daily. Half of new cases are young people aged 15-24 years, 10% of them are children younger than 15 years, and 40% are women. Two thirds of all cases are in the sub-Saharan Africa where the prevalence of the infection reaches 20% in some regions. Since 1981, HIV has killed 11.7 million people including 2.7 million children aged below 15 years. In 1997, 2.3 million deaths of HIV occurred, i.e., five deaths per minute.

Available means for preventing HIV spread are mainly directed towards modification of risk behavior and, at best, provided that the costly combination therapy is widely used (including azidothymidine and its derivatives, viral protease inhibitor, and other drugs that reduce viral load and delay AIDS development), they allow to reduce the risk of new infections twofold during time period ranging from 5 to 10 years, as estimated by the European Center of AIDS Epidemic Monitoring. The irreversibility of HIV spread throughout the world observed so far is caused, in the first place, by the lack of means of vaccination and radical treatment. Until recently, the general belief was that there are even no prerequisites necessary to develop HIV vaccine. At present, the development of such vaccine is considered to be feasible. Moreover, the necessity of HIV vaccine development is recognized at the level of international policy. The corresponding paragraph is included in the final communique of the Denver meeting of leaders of eight industrialized countries, Russia included, that was held in June 1997.

At the same time, it is important to appreciate that HIV vaccine is the most difficult to develop among all vaccines being designed at present. With respect to the nature of infection, the degree of antigenic variability of its causative agent, the existence of the natural immunity, the availability of animal models, and the possibility to culture infectious agent, the score estimate for HIV vaccine difficulty is 14 (maximal possible), whereas it is 9-10 for vaccines against herpesviruses and 6 and 7 for already existing vaccines against measles and polio, respectively. The annual expenditures on HIV vaccines projects currently run in USA and Western Europe are about \$ 200 million, and total costs of existing HIV vaccine projects are in the range of \$ 350-500 million (IAVI Blueprint estimate). It is reasonable to think that all these expenditures will be included in the final cost of a vaccine developed. Therefore, the use of any foreign vaccine is most likely to be rather costly.

The practicability of the development of a domestic HIV vaccine in Russia also follows from some additional considerations. The combination of different HIV-1 subtypes present in Russia is peculiar in that it is more reminiscent of Africa than of USA or Western Europe. On one hand, this makes it less likely that HIV vaccines developed in USA or Europe will be suitable for Russia. On the other hand, this means that the results of Russian domestic vaccine development may be applicable in Africa where the need for HIV vaccine is extreme. It should be also taken in consideration that one of major objectives for an HIV vaccine is that it has to be inexpensive and available for the poorest countries. Russia has gained a considerable experience of solving large-scale problems like that. In particular, global smallpox eradication was accomplished by the initiative of USSR and by means of a vaccine made in USSR. The aforesaid makes reasons to believe that the international community may get interested in Russian HIV vaccine Project enough to give it some financial support. Finally, among former USSR republics under the threat of a full-blown HIV/AIDS epidemic, only Russia has real facilities and the start reserve for the development of HIV vaccine, which places a special responsibility on this country.

Vaccine development makes sense only on the condition that it will be used efficiently. This means that populations should be vaccinated that are under the highest risk of HIV infection, i.e., IDUs, homosexuals, commercial sex workers, promiscuous people, etc. On the other hand, people have to be protected who are under the occupational risk of being exposed to HIV, health care professionals in the first place. Therefore, vaccine development must be backed up by sociological and psychological studies of risk groups to make them accessible for vaccine testing and vaccination.

In parallel with this work, all possible preventive measures should be taken that could change risk behavior so as to slow down HIV spread before vaccination is possible. This will require development on an adequate legislation.

Finally, the development and realization of the aforesaid implies the necessity of further education and training (retraining) of professionals able to appreciate all aspects (biological, medical, economical, legal, etc.) of HIV/AIDS as a systemic biosocial phenomenon.

To sum up, the objectives of the project are to develop an HIV vaccine and make conditions for its efficient use which is the only means that allow not only to slow down HIV spread in Russia but, also, to successfully fight against HIV infection. Besides, with such a vaccine Russia may help its neighbor states and contribute to the solution of the HIV/AIDS problem on the global scale.

2.2. The start reserve

Russian HIV vaccine project is currently operating within the framework of the Federal Russian Program “New Generation Vaccines and Diagnostic Means of the Future”.

By now, the infrastructure of research institutions has been developed. It has a significant start reserve including the following: data on major HIV-1 serotypes and subtypes present in Russia; banks of HIV proteins and respective genes; original methods of obtaining adjuvants and interleukins; know-how of final pharmacy form and vehicle production (microspheres and molecular system of targeted delivery of immunodominant HIV peptides to antigen-presenting cells of the immune system); and general immunological, virological, and other techniques needed for vaccine development and production. The major components of the infrastructure are Biomedical Center (St. Petersburg) and research teams from leading Russian scientific institutions including State Research Center of Virology and Biotechnology known as Vector Laboratories (Koltsovo, Novosibirsk Region), Research Institute of Pure Biochemicals (St. Petersburg), State Research Center of Applied Microbiology (Obolensk, Moscow Region), Institute of Immunology (Moscow), Institute of Applied Research of Moscow State University (Moscow), and D. I. Ivanovskiy Institute of Virology (Moscow). These institutions possess laboratory premises and up to date equipment, which, however, needs significant modernization.

2.3. Project type

The project, as concerned with basic research and preclinical and clinical trials of HIV vaccine, does not imply significant construction activities. Some reconstruction of existing premises may be required. Purchasing of equipment and laboratory supplies will be necessary.

As concerned with vaccine production, new construction will be required. However, for this purpose the engineering block and unfinished production blocks of Research Institute of Pure Biochemicals (St. Petersburg) may be used.

2.4. Major studies and work required to organize and accomplish the project

The following has to be done within the framework of the project:

- to continue studies of the genetic variability of HIV present in Russia and CIS countries, because the vaccine to be developed must contain epitopes present in all major HIV subtypes circulating in these territories;
- to conduct studies needed to design and choose promising immunizing agents and other vaccine components, including immunizing agents based on the smallpox vector, recombinant and/or synthetic peptides, artificial immunizing agents, DNA vaccines, and the killed virus;
- to design immunization schemes that evoke long lasting humoral and cellular immune responses involving mucous immunity;
- to develop original adjuvants and means of preparation of endogenous mediators of the immune response (for example, interleukins);
- to develop final pharmacy forms including efficient delivery means, such as liposomes or/and microspheres and molecular means of targeted delivery based on non-toxic components of bacterial toxins;
- to design a system for stimulating the CD8⁺ cell-dependent immunity by means of recombinant attenuated vaccinia viruses with built-in determinants of epitopes of major HIV strains present in Russia or by means of the same peptide epitopes fused with molecular carriers capable of presenting the epitopes to MHC I molecules present on antigen-presenting cells;
- to study the feasibility of developing tablet and suppository pharmacy forms;
- to study the feasibility of the development of the therapeutic vaccine, in addition to the preventive vaccine;

- to conduct preclinical trials of candidate HIV vaccines using small laboratory animals and to test vaccine efficiency using *Macaca mulatta* challenges with SHIV as the model
- to manufacture experimental batches of HIV vaccine for clinical trials;
- to conduct phase I, II and III clinical trials of HIV vaccine of choice;
- to develop the industrial technology of HIV vaccine production;
- to organize the industrial production of HIV vaccine;
- in order to develop an optimal vaccination strategy, to establish cooperative relations with major risk groups, to determine the order, schedule and scale of vaccination, and to provide other conditions for vaccination;
- to proceed with designing and implementation of measures aimed at the prevention of HIV spread during the period of HIV vaccine development;
- to design and implement the program of education and training (or retraining) of professionals endowed with the knowledge and skills in such disciplines as biology, medicine, sociology, psychology, economics, law, and others needed for the complex approach to questions associated with the HIV/AIDS problem, including those of AIDS vaccination.

2.5 Dislocation of sites of working on the project

Because major forces of the project, Biomedical Center and Research Institute of Pure Biochemicals, are located in St. Petersburg, this city will be the principal project site.

The said institutions are experienced in working on the HIV/AIDS problem; they are staffed with trained personnel and possess an appropriate infrastructure.

The team of Biomedical Center headed by Dr. A. P. Kozlov was among the first to identify cases of HIV infection in Russia and to obtain Russian HIV isolates. The team reported on the first death of AIDS in Russia and described the molecular epidemiology and virology of the nascent phase of HIV/AIDS epidemic in Russia. Finally, this is the team that has designed and proposed the project of Russian HIV vaccine development.

2.6. Additional information for an investment project

HIV vaccine is a novel product. By now, no vaccines of that sort exist. According to prognoses for the number of HIV-infected people in the world by the year 2000, which are from 40 to 100 million people, the demand for HIV vaccine immediately after it is developed will be 100 million doses globally and several million doses in Russia and CIS states.

Some results of the project are likely to be patented. A part of basic components meant to be included in the final product are patented in Russia and abroad. Further patenting of products and relevant technologies is expected. Marketing of licenses concerning separate technological elements or the whole technological process is likely.

Production cycle is supposed to be several months.

Presumable markets include India, Thailand, Africa (especially Equatorial Africa), Latin America, Russia, and other SIC countries.

The price of an HIV vaccine has to be affordable for the developing countries which implies negotiations with WHO, major financial agencies, banks, and governments about the mechanisms of distributing the vaccine.

2.7 Organizational and legal aspects

To make the management of the project more efficient, it is proposed to finance it through a special fund provisionally titled "Fund for Promoting HIV/AIDS Studies". It is expected that the fund will facilitate mobilization of finances from different sources (i.e., budgets of different levels, private sector, and international banks and programs) and to coordinate everything concerned with backing the project.

The fund is expected to make contracts with the principal participant of the project for the accomplishment of R&D work and the creation of scientific and technological products and to make all other contracts required.

The issues of the rights for the intellectual property expected to be created in the process of the accomplishment of this project, i.e. the figure of the patent owner, the members of the collective author, the procedure of royalty allocation, and, also, the issues of managing new business which is likely to emerge have to be scrutinized in the course of elaborating the project.

2.8. The participants (the principal participant and the scheme of interaction between participants)

The principal participant of the project is a St. Petersburg-based autonomous non-commercial organization (ANO) Biomedical Center, a non-governmental research organization which is currently the leading participant of the Russian HIV Vaccine Project.

ANO Biomedical Center is staffed by experienced researchers. At its disposal it has laboratory premises with modern equipment and a well-appointed office with personnel including lawyers and information technology professionals capable of dealing with a broad range of tasks. For example, starting from 1991 Biomedical Center runs annual international conferences "AIDS, Cancer and Related Problems", which is a unique event in Russia. Since 1997, it publishes "Russian Journal of HIV/AIDS and Related Problems", the only Russian professional publication specialized in the problem of HIV/AIDS.

Besides, the work on the project will be performed by research teams that currently participate in studies within the framework of the aforesaid program. The teams are from the following research institutions: State Research Center of Virology and Biotechnology (Koltsovo, Novosibirsk Region), Research Institute of Pure Biochemicals (St. Petersburg), State Research Center of Applied Microbiology (Obolensk, Moscow Region), Institute of Immunology (Moscow), Institute of Applied Research of Moscow State University (Moscow), and D. I. Ivanovskiy Institute of Virology (Moscow).

The participants will interact with ANO Biomedical Center on the contract basis. It is presumed that the procedure of interaction will be based on what has been worked out in the course of the implementation of the aforesaid program and is characterized by that the intermediate accounting includes not only reports but, also and more importantly, samples of production, which are checked in the laboratories of the principal participant and deposited in a special bank. In this way the real course of implementing the program will be controlled and actual results will be appraised.

In regard to the part of the project concerned with the designing of an optimal use of HIV vaccine for performing vaccination in Russia, its principal participant will be a St. Petersburg-based organization "Association against HIV/AIDS". This social agency is one of the organizers of annual international conferences "AIDS, Cancer, and Related Problems" that are run in St. Petersburg since 1991 and summon leading Russian, European, and American authorities in the field of dealing with HIV/AIDS. The activities of this organization were highly appraised by the State Duma in its recommendations worked out in the course of parliament hearing on the theme "On urgent measures for struggling against the spread of AIDS" held on June 8, 1998. The recommendations include the claim that the organization of AIDS Center of the Commonwealth of Independent States is necessary and that this should be done in St. Petersburg on the basis of Association against HIV/AIDS. The Association is renowned internationally. It was the only Russian organization that signed the International Call for Actions to Develop HIV vaccine presented at the Denver Meeting of Leaders of Eight Industrial Countries held in June 1997.

The general course of the work on the project will be discussed at regular workshops timed to annual international conferences "AIDS, Cancer, and Related Problems".

2.9 Provisional analysis of possible risks

The major risk is the possible failure to develop a potent and inexpensive HIV vaccine. However, at present most experts believe that the development of an HIV vaccine is feasible. Main lines to follow in the course of this work are determined. Currently, scores of companies are engaged in this work. At the 12th World AIDS Conference held in Geneva on 25 June - 3 July 1998 the development of HIV vaccine was recognized as the highest priority in controlling HIV/AIDS.

Adverse side effects of different vaccines are known. However, approaches exist to the detection and prevention of such reactions in the course of preclinical and clinical trials. The absence of any specific adverse effects of immunizing volunteers with recombinant HIV-1 proteins has already been demonstrated.

Some risk is represented by that an immunized person becomes seropositive and may be recognized as HIV-infected in screening for HIV conducted by means of traditional methods. However, approaches exist that provide for the differential diagnostics of seropositivity associated with HIV-infection or immunization with HIV vaccine. Nevertheless, legal regulations concerning these aspects of vaccination against AIDS should be worked out.

2.10. Terms of implementation of the project

It is generally believed that the schedule time of an HIV vaccine project is about 12 – 14 years, including clinical trials and design and construction of large-scale production facilities. Basic research is expected to take about five years.

2.11 Provisional schedule of the project

The provisional schedule of the project presented below is designed with account to the under-way work on the development of HIV vaccine performed according to the Russian HIV Vaccine Project

Stage	Period
Studying the genetic diversity of HIV in Russian Federation and CIS countries. Collecting banks of sera and DNA of HIV-positive subjects. Monitoring the HIV/AIDS molecular-epidemiological situation in the regions.	2000-2011
Studying HIV pathogenesis. Adaptation of methods for evaluating immune responses to HIV. Development and introduction of methods for differentiating HIV-infected and HIV-vaccinated humans.	2000-2007
Development of immunizing agents, adjuvants, and delivery vehicles.	2000-2007
Designing the strategy of using HIV vaccine for vaccination in Russia. Development of infrastructure that could provide for reaching risk groups and taking measures aimed at changing risk behavior.	2000-2012
Preclinical trials of candidate HIV vaccines using small laboratory animals.	2001-2004
Developing of the infrastructure for work with SHIV. Preclinical trials of candidate HIV vaccine efficiency using <i>Macaca mulatta</i> challenged with SHIV	2002-2004
Manufacturing of experimental batches of HIV vaccine for clinical trials.	2003-2010
Phase I clinical trials (vaccine safety in humans).	2004-2006
Phase II clinical trials (vaccine immunogenicity in humans).	2006-2008
Phase III clinical trials (protective efficiency of vaccines).	2010-2012
Designing the technology of large-scale vaccine production.	2008-2010
Building facilities for vaccine production.	2012-2013
Vaccine production to provide for vaccinating risk populations in Russia.	2014

3. Requirements for investments and/or guaranties for credit repayment

The total amount of investments required for the implementation of the project is US \$ 160 million.

Backing to be requested from IBRD is US \$ 150 million.

Backing from the Federal Budget of Russia as concerns the Interagency Program “New Generation Vaccines and Future Diagnostic Means” which partly covers the basic research is expected to be equivalent to US \$ 10 million.

Financing by stages

Stage	Financing (US\$, million)
2000–2004	55
2005–2009	53
2010–2014	52
Total:	160, of which 152 from IBRD 8 from RF Federal Budget

PROVISIONAL ESTIMATE OF EXPENDITURES BY LINES OF ACTIVITIES

LINE OF ACTIVITIES	TIME PERIOD/ DURATION (YEARS)	EXPENDITURES (US \$, MILLION)
1. Studying the genetic diversity of HIV in Russian Federation and CIS countries. Collecting banks of sera and DNA of HIV-positive subjects	2000-2011/ 12	12
2. Studying HIV pathogenesis. Adaptation of methods for evaluating immune responses to HIV. Development of means for differentiating HIV-infected and HIV-vaccinated humans means.	2000-2007/ 8	8
3. Developing the immunizing agents, adjuvants, and vehicles.	2000-2003/ 4	9
4. Designing a strategy of using HIV vaccine for performing vaccination in Russia.	2000-2012/ 13	12
5. Preclinical trials of candidate HIV vaccines using small laboratory animals	2001-2004/ 4	8
6. Developing of the infrastructure for work with SHIV. Preclinical trials of candidate HIV vaccine efficiency using <i>Macaca mulatta</i> challenged with SHIV	2002-2004/ 3	12
7. Manufacturing of experimental batches of HIV vaccine for clinical trials.	2003-2010/ 8	23
8. Phase I clinical trials	2004-2006/ 3	12
9. Phase II clinical trials	2006-2008/ 3	12
10. Phase III clinical trials	2008-2011/ 4	16
11. Development of technology for large-scale vaccine production	2010-2012/ 3	20
12. Constructing of facilities for vaccine production.	2012-2013/ 2	18
13. Vaccine production for the first bout of vaccination in Russia	2014/ 1	10

<u>Total:</u>	US\$ 160 million, of which US\$ 152 million from IBRD US\$ 8 from RF Federal Budget
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First stage: years 2000-2004

LINE OF ACTIVITIES	TIME PERIOD/ DURATION (YEARS)	EXPENDITURES (US \$, MILLION)
1. Studying the genetic diversity of HIV in Russian Federation and CIS countries. Collecting banks of sera and DNA of HIV-positive subjects	2000-2004/ 5	5
2. Studying HIV pathogenesis. Adaptation of methods for evaluating immune responses to HIV. Development of means for differentiating HIV-infected and HIV-vaccinated humans means.	2000-2004/ 5	6
3. Developing the immunizing agents, adjuvants, and vehicles.	2000-2003/ 4	9
4. Designing a strategy of using HIV vaccine for performing vaccination in Russia.	2000-2004/ 5	5
5. Preclinical trials of candidate HIV vaccines using small laboratory animals	2001-2004/ 4	8
6. Developing of the infrastructure for work with SHIV. Preclinical trials of candidate HIV vaccine efficiency using <i>Macaca mulatta</i> challenged with SHIV	2002-2004/ 3	12
7. Manufacturing of experimental batches of HIV vaccine for clinical trials.	2003-2004/ 2	6
8. Phase I clinical trials	2004/ 1	4
<u>Total:</u>	US\$ 55 million, of which US\$ 52 million from IBRD US\$ 3 from RF Federal Budget	

Second stage: years 2005-2009

LINE OF ACTIVITIES	TIME PERIOD/ DURATION (YEARS)	EXPENDITURES (US \$, MILLION)
1. Studying the genetic diversity of HIV in Russian Federation and CIS countries. Collecting banks of sera and DNA of HIV-positive subjects	2005-2009/ 5	5
2. Studying HIV pathogenesis. Adaptation of methods for evaluating immune responses to HIV. Development of means for differentiating HIV-infected and HIV-vaccinated humans means.	2005-2007/ 3	2
3. Designing a strategy of using HIV vaccine for performing vaccination in Russia.	2005-2009/ 5	4
4. Manufacturing of experimental batches of HIV vaccine for clinical trials.	2005-2009/ 5	14
5. Phase I clinical trials (1 st and 2 nd years)	2005-2006/ 2	8
6. Phase II clinical trials	2006-2008/ 3	12
7. Phase III clinical trials	2008-2009/ 1	8

	2	
Total:	US\$ 53 million, of which US\$ 50 million from IBRD US\$ 3 from RF Federal Budget	

Third stage: years 2010-2014

LINE OF ACTIVITIES	TIME PERIOD/ DURATION (YEARS)	EXPENDITURES (US \$, MILLION)
1. Studying the genetic diversity of HIV in Russian Federation and CIS countries. Collecting banks of sera and DNA of HIV-positive subjects	2010-2011/ 2	2
2. Designing a strategy of using HIV vaccine for performing vaccination in Russia.	2010-2012/ 3	3
3. Manufacturing of experimental batches of HIV vaccine for clinical trials.	2010/ 1	3
4. Phase III clinical trials	2010-2011/ 2	8
5. Development of technology for large-scale vaccine production	2010-2012/ 3	8
6. Constructing of facilities for vaccine production.	2012-2013/ 2	18
7. Vaccine production for the first bout of vaccination in Russia	2014/ 1	10
Total:	US\$ 52 million, of which US\$ 50 million from IBRD US\$ 2 from RF Federal Budget	

The advance needed to finally elaborate the project makes US \$ 500 000.

4. Project efficiency

The main criterion of the efficiency of the project is the ultimate possibility to prevent a large scale HIV/AIDS epidemic in Russia, which will result in the reduction of state subsidy for settling the consequences of the epidemic.

The level of this subsidy may be tentatively estimated basing on the following:

- according to WHO recommendation, the annual cost of servicing one AIDS patient is US \$ 20 000;
- the cost of life long maintenance of one HIV-infected subject varies from \$ 20 000 in Africa to \$ 119 000 in USA (according to NIAID data);
- by now, the total cost of HIV/AIDS epidemic in Africa is \$ 30 billion;
- the United States have already spent \$ 75 billion to fight against HIV/AIDS and spend from \$ 3 billion to \$ 6 billion each year because of new cases of HIV infection;
- total HIV/AIDS-caused losses for the world economy are expected to reach \$ 514 billion by the year 2010;

It should be added that the adequate antiviral therapy of all HIV-infected subjects in Russia requires about one ton of azidothymidine annually, the price of the drug being about \$ 60 per package containing 100 0.1 g tablets, which makes \$ 6 million annually. The purchasing of an imported preparation of the drug (say, Glaxo-Welcome) will cost thrice as much.

Another interesting fact is that in 1997 the US Government has spent \$ 130 million for the studies concerning HIV vaccine, whereas the Government of Brazil spends a similar sum of money each year for antiviral drugs (azidothymidine and others).

Therefore, HIV vaccine development not only will be the radical solution of the HIV/AIDS problem but, in the long run, it will be a much more efficient solution of the problem from the point of view of economy. This is especially true for countries, Russia included, that back the major portion of health care with their state budget. Moreover, because the number of possible but vaccine-prevented cases of HIV-infection will increase each year, the positive economic impact of HIV vaccine will increase, too.

Another economic aspect of HIV/AIDS epidemic is that the disease mainly affects the most active employable population. In Africa, where up to 25% of people are infected in some areas, there are countries that are already experiencing economic problems caused not only by direct expenses for the consequences of the epidemic but, also, by the lack of hands.

It follows from the above that the prevention of a large-scale HIV/AIDS epidemic in a country like Russia will have significant geopolitical consequences, in particular, it will create a favorable climate for investments in Russian economy in the XXI century.

The possible export of HIV vaccine to developing countries is not taken into account in these estimates

5. Ecological impact of the project

5.1. Project category from the viewpoint of possible adverse effects on the environment

During vaccine development no impact from the research on the environment is expected.

At the stage of vaccine manufacturing the technology is expected to be environmentally safe.

5.2. The scale of the impact on the environment

Any possible impact on the environment will be local, i.e., within sites of vaccine manufacturing.

5.3. Nature management status at the sites of implementing the project

The sites of implementing the project are not under special environmental protection.

5.4. Possible environmental pollution resulting from the implementation of the project

Any possible environmental pollution is within the range typical for the manufacturing of health care products.

5.5. Conformity to environmental regulations

All the work on the implementation of the project will be done in conformity with environmental regulations.

5.6. Expected increase or decrease in waste product generation

No significant waste product generation is expected.

6. Social impact of the project

By the judgment of World Bank experts (the program report on World Bank study "Face to Face with AIDS: Priorities of the World Society Challenged by the Global Epidemic", the struggle against HIV/AIDS is one of the key problem of human development. This judgment is based on that

HIV/AIDS epidemic dramatically worsens such integral criteria of well-being as human longevity, public health, and economic growth.

The above implies that the present project is of a high social significance associated, first of all, with the prevention of a large scale epidemic with the potential of making hundreds of thousands people to die in Russia.

Besides that, the realization of this project will allow to preserve and advance the scientific potential of leading Russian institutions making research in the field of molecular biology and biotechnology. Technologies developed in the course of working on the project will be used further to develop means for the diagnosis, prevention, and treatment of a wide range of other diseases, including emerging and reemerging infections. This will provide for a better health care and people's well-being in Russia.

The realization of the problem involves the introduction of a range of social innovation including the establishment of new type relations with HIV-infected people and risk groups. On the whole, all that will result in the decrease of the incidence and prevalence of infections, including sexually transmitted diseases.

Table 1 Candidate HIV vaccines

IMMUNIZING AGENT	DESCRIPTION	DEVELOPER
Artificial immunizing agents		
TBI-1	Gag and Env epitopes	Vector Laboratories
TCI	Gag, Env, Pol, and Nef Epitopes	Vector Laboratories and Research Institute of Pure Biochemicals
MAP-systems incorporating synthetic V3-peptides	Epitopes of the V3-loop of different HIV-1 subtypes	Research Institute of Pure Biochemicals
Recombinant poxvirus		
Vaccinia-virus based	Gag and Env epitopes	Vector Laboratories and Research Institute of Pure Biochemicals
DNA-based HIV vaccines		
PCMV-env-1	Env	Research Institute of Experimental Medicine, Research Institute of Pure Biochemicals and Biomedical Center
PMO-env-1	Env	Research Institute of Pure Biochemicals and Biomedical Center
Multiepitope DNA-based vaccines of the pBMC series	Gag, Pol, Env	Research Institute of Pure Biochemicals and Biomedical Center
Killed virus		
Lysed HIV	Complete set of HIV protein	Ivanovskiy Research Institute of Virology, Vector Laboratories, and Research Institute of Pure Biochemicals
Inactivated HIV virions	Complete set of HIV protein	
Vehicles for the delivery of immunizing agents to the organism		
Fused protein containing anthrax toxin fragments	Env, p17, p24	Research Institute of Applied Microbiology and Biomedical Center
Microspheres	DNA-vaccine, TBI	Research Institute of Pure Biochemicals
Complex of DNA with poly-(L-lysine-lactoferrin)	DNA-vaccine	Research Institute of Pure Biochemicals, Research Institute for Experimental Medicine
Liposomes	DNA-vaccine, TBI	Research Institute of Pure Biochemicals
Salmonella-based HIV vaccines		
A non-virulent <i>Salmonella typhimurium</i> strain containing plasmid with TBI gene	Gag and Env epitopes	Sechenov Medical Academy, Vector Laboratories, Biomedical Center
A non-virulent DNA-vaccine-containing <i>Salmonella typhimurium</i> strain	Gag, Pol and Env epitopes	Biomedical Center
Novel adjuvants for the development of HIV vaccine		
Polyoxidonium	Synthetic proteins and peptides	Research Institute of Immunology
Lactolen (pentopeptide glycan)	Synthetic proteins and peptides	Research Institute of Pure Biochemicals