The Unique U.S.-Russian Relationship in Biological Science and Biotechnology: Recent Experience and Future Directions

DETAILS

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The Unique U.S.-Russian Relationship in Biological Science and Biotechnology

RECENT EXPERIENCE AND FUTURE DIRECTIONS

Committee on U.S.-Russia Bioengagement

Development, Security, and Cooperation

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Tens of thousands of scientists and other specialists from the United States and Russia have participated in bilateral bioengagement activities in recent years. Their contributions to science, security, public health, agricultural productivity, environmental protection, and other important areas that sustain life have been profound. The committee is grateful for the opportunity to prepare a report on their contributions to society. The committee is particularly appreciative of the insights provided specifically for this report by many officials, scientists, and program managers who participated in the activities or witnessed their implementation in the two countries.

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Academies' Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the process.

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Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of this report was overseen by Edwin Przybylowicz, Eastman Kodak Company (retired). Appointed by the National Academies, he was responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

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Summary

In the fall of 2010, the U.S. National Academies (consisting of the National Academy of Sciences, the National Academy of Engineering, the Institute of Medicine, and the National Research Council) and the Russian Academy of Sciences (in cooperation with the Russian Academy of Medical Sciences and the Russian Academy of Agricultural Sciences) initiated a joint study of U.S.-Russian bilateral engagement in the biological sciences and biotechnology (hereinafter collectively referred to as bioengagement). The U.S. Department of State and the Russian Academy of Sciences provided support for the study. The academies established a joint committee of 12 leading scientists from the two countries to assess bioengagement activities since 1996 and to provide recommendations as to collaborative efforts in the near future. The principal conclusions and recommendations of the study are set forth in this summary and are elaborated in the complete report.

Shared health, agricultural, and environmental interests of the United States and Russia, together with common security concerns, involve activities of national and international interest spread over vast ecological landscapes that cover 34 percent of the land surface of the northern hemisphere. The countries have two of the world's largest scientific work forces, skilled in virtually all aspects of the life sciences. Their specialists have repeatedly demonstrated how bioengagement can advance science, contribute to economic and social progress, and promote international security. Many of these scientists have developed long-term professional and personal relationships across the ocean that have helped advance their scientific capabilities and broaden their global perspectives. The two countries are now well positioned to capitalize on joint achievements of the

past while pursuing emerging bioengagement opportunities that can continue to benefit both countries.

Looking to the future, the Russian government is in the process of terminating Russia's involvement in the Cooperative Threat Reduction Program administered by the U.S. Department of Defense (often referred to as the Nunn-Lugar Program), the foreign assistance efforts of the U.S. Agency for International Development, and the activities of the International Science and Technology Center. These three programs have provided important pillars of U.S.-Russian bioengagement efforts for many years. But during the past several years the U.S. government has significantly reduced financial support for bioengagement through these and other channels in favor of competing budget priorities.

Despite the foregoing developments, the committee responsible for this report considers that the case is strong for expanding U.S.-Russian bioengagement, even in the face of budget stringency by both governments. The stakes are significant, the established base for collaboration is unprecedented, and many of the potential payoffs from future joint efforts are clear. The broad-ranging assessment in this report of lessons learned and of future collaboration opportunities should help ensure that the governments and the scientific leaders in both countries now give adequate attention to the many dimensions of and rewards from U.S.-Russian bioengagement.

BIOENGAGEMENT IN THE LATE 1990s AND EARLY 2000s

Following the splintering of the Soviet Union into 15 independent states, officials in Washington, Brussels, and other western capitals, in cooperation with Russian government counterparts, launched a number of bilateral and multilateral programs to help limit internal and external brain drains of Russian scientists whose salaries were no longer adequate for meeting even minimal needs. A particular concern was the possibility that Russian scientists with important nuclear, biological, chemical, or aerospace skills who were facing difficult economic problems might accept financial support from nefarious sources interested in using Russian expertise for dangerous purposes. At the same time, scientists in the West, as well as their colleagues in Russia, were apprehensive that without an infusion of financial resources from abroad, civilian-oriented capabilities of Russia's scientific institutions that were of international significance would decline and eventually be lost.

In a few years, bioengagement reached unprecedented heights. The U.S. government provided substantial financing. Russian institutions that were interested in bioengagement provided important matching resources along with their extensive knowledge base. Since the mid-1990s, U.S. and Russian organizations have invested more than **$1 billion** in bioengagement, with the U.S. side covering most of the direct costs. The Russian side has covered many of the indirect expenses, such as costs of utilities, facility improvements, program management and documentation, and other overhead expenses, as well as provided most of the scientific expertise. Much of the funding and expertise has been linked to (a) proliferation concerns of both countries and (b) health components of the U.S. foreign assistance program.

Bioengagement had a profound effect in preserving important segments of the research infrastructure of Russia during times of severe economic difficulties. Thousands of Russian life scientists who participated in joint projects had new opportunities to contribute to (a) advancement of science, (b) applications of scientific findings leading to better and cheaper products and improved services that help meet the needs of the population, and (c) assessments of important health, agricultural, and environmental issues of regional and global significance. At the same time, hundreds of American scientists have benefited from collaborations with Russian colleagues whose expertise, experience, and access to territories, facilities, and data banks had been little known outside Russia.

REVITALIZATION OF RUSSIA'S CAPABILITIES

Currently, Russia is reshaping its scientific infrastructure. Several hundred Russian biology-oriented research laboratories are now well equipped and staffed to work at an international level. Many more health, agricultural, and environmental facilities provide updated services with broad-ranging benefits for important segments of the population. Russian scientific publications in internationally accredited journals, while still very limited in number, are commanding increased scientific interest.

At the same time, emigration of outstanding young Russian scientists in recent years has been a serious loss that limits Russia's scientific capabilities. Today a new generation of well-educated young professionals with up-to-date skills and interests is slowly filling important gaps in the availability of technical personnel in the country.

In most areas of the biological sciences and biotechnology, the United States is technologically more advanced than Russia. Also, scientists working in U.S. facilities, with broad access to modern equipment and to skilled technical support staffs, are generally able to work more efficiently than counterparts in Russia. This gap arises not only because science is better financed in the United States than in Russia but also because U.S. scientists have more experience in managing research activities that yield results suitable for application in a market economy.

Substantial financial support of U.S. science also (a) helps ensure stability of the technical workforce and (b) provides broad opportunities for international connectivity of scientific centers. Moreover, in the United States there has been a consistent focus on strengthening basic research capabilities. In this regard, an important U.S. priority has been providing opportunities for scientists in the early stages of their careers to become important participants in exploring unfolding fields of science.

In a number of subfields, Russian scientists are making contributions at the forefront of the life sciences. Russian achievements, when coupled with U.S. strengths, often offer important synergistic effects in advancing capabilities of both countries to work effectively in these subfields, such as enhancing understanding of the characteristics of the influenza A/H5N1 virus. When projects focus on conditions in specific geographical environments, each country has unique experience that combined may offer remarkable scientific insights that would not otherwise be possible.

IMPACTS OF BIOENGAGEMENT

The investments of the United States and Russia in bioengagement during the past 15 years are paying off in important ways. Communications between counterparts have been commonplace, addressing not only the details of joint projects but also broader professional interests. As a result, the development of unique research approaches has been frequent, and research findings of joint efforts have been significant.

At times, working together has dramatically reduced preconceived suspicions about the possibility of inappropriate intentions of the leaders of previously closed scientific facilities in the two countries. Transparency and insights as to accomplishments and future plans have increased greatly. It is important for both countries and for the advancement of science more broadly that the personal relationships that have led to openness and confidence building over the years be maintained.

Significant public- and private-sector organizations in the two countries are now well positioned for and interested in intensifying research collaboration that would benefit both countries. Also, following a long period of hesitation, a few entrepreneurial investors in the two countries have taken initial steps to develop joint commercial opportunities in the biotechnology marketplace.

Of particular significance has been "working together" in the development of effective approaches for (a) ensuring biosafety when handling dangerous pathogens, (b) improving disease surveillance capabilities, (c) reducing the prevalence of agricultural pests and pathogens, and (d) assessing and reducing environmental problems. American and Russian colleagues are now well prepared to continue their cooperative efforts more effectively than during their initial pioneering experiences. The likely positive impacts of collaboration certainly deserve appropriate recognition by the two governments in their policy and budget decisions affecting bioengagement.

At the policy level, the U.S.-Russia Bilateral Presidential Commission established in 2009 has provided an important mechanism for encouraging political support of new bioengagement initiatives, as well as for coordinating and facilitating ongoing collaborative programs.

NEW RUSSIAN INVESTMENTS

As previously noted, during the past several years, there has been a steady decline in the extent of bioengagement. The United States has shifted much of its financial resources from programs centered in Russia to programs sited in other areas of the world. The Russian government has only slowly followed through on long-standing commitments to share more fully the direct costs of bioengagement activities that benefit both countries.

Meanwhile, the Russian government has initiated a number of new programs, with mandates for international outreach. One priority area is the biomedical field. The other priorities are nuclear, space, information, and energy technologies. Activities of special interest are the following:

- The Skolkovo Foundation is supporting the establishment of a flagship high-technology education-research complex headquartered near Moscow, which is being designed with the participation of the Massachusetts Institute of Technology.
- The Skolkovo Foundation also provides research and development grants in the five priority areas listed above, primarily to Russian companies, with occasional involvement of Russian institutes and universities working with international partners. These partners receive tax exemptions, customs privileges, and other incentives that encourage their participation.
- Rusnano, which is supported by the Russian government, is providing grants and contracts to Russian companies and also at times to institutes and universities for activities that are designed to lead to near-term commercialization of nanobiotechnologies, drawing on the experience of the United States and other countries when considered appropriate.
- Russian government-supported venture funds are investing in U.S.-based start-up and established companies, including biotech companies, which in turn will engage both commercial and research organizations based in Russia.
- The Kurchatov Institute of Atomic Energy, heralded as the country's first national laboratory, is expanding its new nanobiology facilities and is seeking relationships with U.S. organizations with common interests.
- In April 2012, the Russian government issued a broad decree calling for establishment of a framework for a national biomedical program (Pharma 2020), although the funding to carry out this program has been uncertain.

It is too soon to assess the importance and impact of these recent activities, which are oriented to promoting Russian scientific and economic interests, including expansion of opportunities for international cooperation. The new types of Russian investments in biomedical activities are planned to reach levels in the tens of millions of dollars annually, and investments are beginning. A number of Russia's leading scientists, including well-known biologists, are participating in the programs. Significantly, the political support of the Russian government for these activities during the next several years seems reasonably assured, which should provide Russia with opportunities to leverage its own investments through international collaboration.

These and other biology-related outreach initiatives of the Russian government emphasize biomedical applications, with most of the government funding provided to companies, including state-owned companies, and to applied research laboratories and service organizations. The basic research capabilities of the country—particularly the capabilities of laboratories that are organizationally linked to the Russian science academies, universities, and research branches of several ministries—also need strengthening, with international collaboration an important mechanism to achieve upgraded capabilities. Leading Russian biologists recognize that a strong and broad basic science infrastructure is essential for development of new drugs, vaccines, and other medical products. But there are skeptics in both Russia and the United States who are not convinced that a broadening of basic research in Russia, in and of itself, will contribute in a significant manner to the "return" on investments made by the Russian government.

Several less ambitious Russian government initiatives have recently been directed toward strengthening research at universities. They include (a) the designation of 29 elite universities as "research universities," with access to special governmental funding, including several universities with well-developed programs in the life sciences and (b) 79 megagrants of $5 million each over 3 years for establishing new research laboratories within the universities. These laboratories are to be led by internationally respected scientists from within Russia and from abroad. However, relatively few of the initiatives targeted on universities have been directed to the life sciences thus far.

In short, in Russia's efforts to improve contributions of the life sciences to economic and social progress, the government has not given adequate priority to strengthening basic research capabilities. To be economically competitive in the long run, public- and private-sector organizations involved in manufacturing and in providing services need a steady infusion of novel ideas and new talent from the nation's basic science and higher education institutions. The traditional focus by the U.S. government on U.S. universities that support the life sciences is now paying off, both in basic and applied science. Meanwhile, Russia continues the important task of strengthening its medical education and applied research complexes. Thus, both countries can gain from one another through bioengagement, although the approach should be tailored to the specific interests and capabilities of the participating institutions.

Of special interest in both countries is nurturing the capabilities of young scientists. Many highly creative young Russian life scientists are now remaining in Russia, where some are attracted by financial incentives offered by emerging and expanding biotech companies. Such newly minted industrial researchers are becoming very focused on near-term applications of existing technologies. This orientation is understandable. But comparable applications of the talents of young scientists in searching for fundamentally new approaches are also important, and the government should strongly support their research activities.

Meanwhile, many U.S. and other western organizations are hesitant to become financially involved in the new biotechnology activities in Russia. A long history of problems in ensuring a business-friendly environment in Russia that provides appropriate protection for financial investments from abroad does not fade easily from memory. Fortunately, Russian partners with good understanding of the importance of responsible handling of international investments are now emerging; and U.S. institutions should be alert to bioengagement opportunities that will avoid difficulties of the past.

Also of significance are Russian capabilities in the life sciences that are not directed to biomedical applications. Hundreds of well-respected university and academy centers direct their attention to basic issues in the agricultural and environmental sciences, often on skimpy budgets. In recent years, opportunities for cooperation in these fields have been manyfold with considerable payoffs for the participants. They continue to deserve attention by organizations in the two countries that have access to funds for outreach programs.

THE FUTURE OF BIOENGAGEMENT

Against a background of declining U.S. financial support for bioengagement programs, strengthened capabilities of Russian institutions to be effective partners, and greater Russian government interest in biotechnology, increased support for future bioengagement deserves careful consideration. Common scientific interests, complementary activities under different but related geographical circumstances, and unprecedented experience of specialists from the two countries in effectively working together for more than a decade are unrivaled. They provide compelling reasons for revitalizing bioengagement activities that include, but extend beyond, a biomedical focus.

The committee responsible for this report concludes that it is clearly in the interest of the United States and Russia for the governments to support a robust bioengagement program, involving both government and private-sector institutions and initiatives. The likelihood of achieving high-value payoffs from carefully designed and well-implemented programs is high. A continued decline in financial support of bioengagement would be a serious mistake, one that should be reversed through joint action of the two governments.

Indicators of success range from joint scientific publications to new trade opportunities to enhanced transparency. Also, of considerable importance is the establishment of lasting personal relationships among scientists with common interests in the responsible use of science for social and economic betterment.

Most of the recent bioengagement programs supported by the two governments have achieved their short-term objectives and have set the stage for follow-on activities. These achievements include (a) strengthened physical security, and particularly biosafety measures, surrounding biological materials of concern; (b) improved protection of the population from the spread of infectious diseases; (c) enhanced agricultural productivity; and (d) upgraded approaches to preservation of ecological resources. Also, the increasing interest of the two governments in working together to encourage private-sector initiatives has been important in encouraging the long-term evolution of a market economy in Russia.

The two governments have decided to terminate most security-driven bioengagement activities, and particularly the enhancement of physical protection of biological materials in Russia, given the strengthened capabilities of the country to address its own internal security concerns. However, the governments recognize that the prevention of proliferation has many dimensions, including providing scientists with defense-related backgrounds with the skills and opportunities to pursue stable civilian-oriented career tracks. Joint programs often indirectly enhance biosecurity, while advancing science. Such programs also can (a) emphasize responsible science when dealing with uncertain technologies in fields such as synthetic biology, (b) encourage greater emphasis on bioethics, and (c) strengthen biosafety. In these areas, U.S. and Russian institutions can and should continue to demonstrate how bioengagement contributes to biosecurity. (For the purposes of this report, biosafety is defined as: "Prevention of exposure to harmful biological agents and measures taken to this end." Biosecurity is defined as: "A complex of measures that include biosafety, while also providing for physical safekeeping of biomaterials and for prevention of inappropriate use of biomaterials.")

No other countries have moved forward from such a pervasive past of suspicion and conflicting objectives than those that characterized U.S.-Russian relations in the early 1990s to an era of confidence and mutuality of program goals that have characterized the U.S.-Russian relationship in recent years. **Thus, the committee's first recommendation is that the two governments support and expand ongoing bioengagement activities that have clearly demonstrated significant scientific and related benefits for both countries.** Currently active cooperative programs are quite limited, funded at a level that supports about 20 percent of the range of activities that were under way a few years ago. Some programs may require modifications, particularly those that were justified in the first instance by their potential to redirect former defense scientists to civilian activities. The best incentive for introducing modifications of past approaches is the likelihood of future funding opportunities that encourage such modifications. In short, a revitalized approach is needed and should be actively pursued.

Second, the committee recommends that the two governments establish a jointly financed new research fund, under the direction of an independent board of directors, with its members appointed by the two governments. The fund should have small offices embedded in existing institutions in both countries, thereby avoiding the complications of establishing new legal entities. The fund should enable American and Russian scientists from interested institutions to join in designing and carrying out projects that enhance important components of the research and development cycle, with special emphasis on basic research activities. This emphasis can provide specialists in both countries access to achievements in the other country that are in the formative stage. Their assessments of developments can best be carried out during onsite discussions and collaboration.

In short, each project supported by the fund should be of scientific interest to and implemented by researchers in both countries working together. To attract both well-established and young scientists and to build lasting networks of researchers with common interests, most projects—selected on the basis of carefully structured peer reviews—should be relatively large (e.g., up to $2 million for 3-year projects) and involve scientists from several institutions. Each side should commit to joint funding; and the financial resources should be disbursed in a coordinated manner, with 50 percent of the overall funds to collaborating institutions in each country, although the division of funding will undoubtedly vary with specific needs from project to project.

Given the breadth of the life sciences and the demonstrated capabilities of the United States and Russia to cooperate effectively in many areas, the annual launch of 15–20 projects over a period of 5 years could effectively engage a number of key laboratories and specialists in important scientific relationships. Highly visible, easily understood, and long-term impacts would be important goals for the projects. Successful efforts very likely would attract additional follow-on support from other national and international sources. Such sources would include, for example, the previously identified new outreach initiatives being developed by the Russian government and the currently latent international interests of the U.S. private sector in research investments in Russia.

Among the topics that are suitable for joint investigations are the following:

- Development of novel therapeutics, diagnostics, drugs, and vaccines.
- Improvements in disease surveillance and monitoring techniques.
- Introduction of new approaches and techniques in synthetic biology.
- Understanding and curtailment of negative influences on animal health and latent zoonotic diseases.
- Measures to control plant diseases.
- Understanding and preservation of biodiversity.
- Research with dangerous pathogens requiring specialized biocontainment facilities and highly experienced staff capabilities.

The committee's third recommendation is that the two governments continue their efforts to reduce the impediments to cooperation. At the top of the list of persistent problems are the difficulties in obtaining appropriate visas for cooperative activities in a timely manner. Current efforts of the two governments to improve the visa situation should continue. Other potential impediments to cooperation relate to tax and customs aspects of joint projects, restrictions on international shipments of biological materials, intellectual property rights associated with joint projects, and compliance with export control requirements.

Introduction

In the fall of 2010, the U.S. National Academies (consisting of the National Academy of Sciences, the National Academy of Engineering, the Institute of Medicine, and the National Research Council) and the Russian Academy of Sciences, in cooperation with the Russian Academy of Medical Sciences and the Russian Academy of Agricultural Sciences, established a joint committee of 12 prominent scientists from the United States and Russia to review past and current U.S.-Russian bioengagement activities and to propose future directions for cooperation that will serve the interests of both countries. (See Appendix A.1 for biographies of committee members.) The U.S. Department of State and the Russian Academy of Sciences supported the committee's efforts.

The Statement of Task that the committee addressed is as follows:

> The committee will carry out an assessment of U.S.-Russian bioengagement activities during the past 15 years, with particular attention to the impacts of various types of engagement activities, lessons learned from engagement activities that are relevant for future U.S.-Russian engagement programs, and future approaches to U.S.-Russian bioengagement, particularly approaches that build on the foundations for cooperation that have been established during recent years.

CONTEXT FOR THE REPORT

For decades, many Russian and American organizations and individual scientists have recognized the importance of working together on a bilateral basis in the biological sciences and biotechnology (hereinafter collectively referred to as bioengagement). Often they have developed and carried out programs within the frameworks of formal intergovernmental agreements. At other times, they have conducted joint activities under a variety of less formal arrangements, ranging from handshakes between individual scientific leaders to institution-to-institution memoranda of understanding.

Collaborative efforts have been broad ranging. For example, they have extended from (a) enhancing biosafety systems at Russian research centers, to (b) fusing biology and chemistry in exploring molecular structures in the laboratories of both countries, to (c) investigating pre-historic microbes in remote areas. The two governments have coordinated laboratory and field investigations to upgrade the systems that help sustain the health of human populations, enhance the value of agricultural resources, and preserve the ecological landscape more broadly. They have collaborated in addressing diseases that can cross international borders—for example, Severe Acute Respiratory Syndrome (SARS), polio, Human Immunodeficiency Virus (HIV), and avian influenza. The joint efforts of individual scientists in preserving important plant, animal, and insect populations, including unique species found throughout the vast territories of Russia, Alaska, and the southwestern United States, are well known within the international biological community.

Following the splintering of the Soviet Union into 15 independent states in 1991, officials in Washington, Brussels, and other capitals initiated a series of bilateral and multilateral programs to help contain the loss or misdirection of Russian scientific expertise. Of particular concern was the possibility that underemployed and poorly paid scientists who had worked in the Russian defense sector might accept financial support from nefarious sources that would pay generously for access to technological expertise that could be used for destructive purposes. Initially, international attention concentrated on the possibility of nuclear scientists going astray; but Russian scientists with biological skills were quickly included in fast-growing cooperative programs to prevent misdirection of advanced technology capabilities. Soon many Russian chemical and aerospace scientists also became involved in international programs to redirect careers to civilian activities of scientists with defense-related experience.

At the same time, there were outcries from U.S. colleagues of prominent Russian scientists, along with loud voices of concern in Europe, that it was essential to save critical components of Russian science, and particularly civilian-oriented basic research capabilities of international interest that had been developed during the Soviet era. The U.S. government responded to the calls from the Russian and U.S. scientific communities for international support by establishing cooperative programs that soon encompassed many aspects of the life sciences, along with programs in other fields. As was to be expected at the time of economic chaos in Russia, the activities initially took on donor-beneficiary characteristics of foreign assistance programs.

Since the mid-1990s, bioengagement has involved many thousands of Russian and hundreds of American scientists, engineers, doctors, industrialists, technicians, and other specialists with important skills. Most participants have been associated with government agencies, research centers, educational institutions, private firms, and nongovernmental organizations in the two countries. Also, a significant number of participants from both countries have been self-motivated entrepreneurs.

As noted above, the two governments initially gave special priority to redirection of Russian research teams with defense backgrounds to civilian careers. An estimated 7,000 Russian specialists with biodefense-relevant expertise and/or experience participated in redirection programs. Most team members remained in their original places of employment, with new job assignments. These programs, together with joint activities based on common scientific interests involving laboratories that had not been entwined with defense activities, contributed to important advances in a number of areas of the life sciences. However, the number and scope of bioengagement programs initiated in response to security concerns have been on the decline during the past several years along with an overall decline in U.S.-Russian cooperation.

Joint efforts, whether motivated by security or other concerns, have often emphasized applications of research findings that can advance social and economic agendas of government departments and private-sector organizations. Collaboration has frequently been oriented toward providing products, technical information, or services of importance to the governments, with commercialization of the products of research in the private-sector marketplace also an objective at times. In addition, bilateral cooperation has addressed the scientific aspects of a variety of global and regional issues of broad interest to the international community, from strengthening global networks for detecting outbreaks of contagious diseases, to husbanding fishery stocks in ocean waters of common interest, to preservation of biodiversity in mountainous areas, to understanding the biological dimensions of climate change.

During the 1990s and into the early 2000s, U.S. government organizations covered most of the direct costs of bioengagement programs, often providing salary support for Russian participants in cooperative undertakings. As to indirect costs—such as providing facilities, utilities and engineering services, retirement and health benefits for employees, and management services, the Russian institutions where projects have been sited carried most of the financial burden.

The most active U.S. government organizations in promoting bioengagement in recent years have included the Department of State (Appendix C.1), Defense Threat Reducation Agency (Appendix C.2), Department of Energy (Appendix C.3), Department of Health and Human Services (Appendix C.4), National Institutes of Health (Appendix C.5), Centers for Disease Control and Prevention (Appendix C.6), and U.S. Agency for International Development (Appendix C.8). The Agricultural Research Service of the Department of Agriculture (Appendix C.10) and the Environmental Protection Agency (Appendix C.9) have also sponsored many joint activities with Russian counterparts. To a lesser extent, the National Science Foundation (Appendix C.7), National Oceanic and Atmospheric

Administration, U.S. Fish and Wildlife Service (Appendix C.11), and Food and Drug Administration have supported collaborative activities involving Russian institutions.

Many Russian institutions have participated in biosecurity- and biosafety-oriented cooperative programs supported financially by the United States. Biosecurity is herein defined as "A complex of measures that include biosafety, while providing for physical safekeeping of biomaterials and preventing inappropriate use of biomaterials." Biosafety is defined as: "Prevention of exposure to harmful biological agents and measures taken to this end."

The jointly implemented programs have usually depended on substantial in-kind contributions from the collaborating Russian institutes, universities, and enterprises. Until recently, special funding from ministries or other organizations to initiate such activities had seldom been available. Of course, when a project terminates, the appropriate ministry, academy, or institution itself must assume responsibility for continuation of the activities, as appropriate.

As to the programs that have not been directly linked to biosecurity concerns, a number of Russian ministries, academies, and special funds have provided support for joint activities (e.g., the Ministry of Health and Social Development, Ministry of Natural Resources, Ministry of Education and Science, and Ministry of Agriculture; three Russian academies; the Russian Foundation for Basic Research; and the Foundation for Support of Small Business in the Science and Technology Sphere—the Bortnik Fund). While they seldom have had major funding earmarked for such activities, they have often been able to allocate a limited amount of support for specific projects. At times, the international departments of ministries and academies have had flexibility in their financial resources to provide support on a case-by-case basis; but usually the interested institutes have been obliged to find the needed resources within their regular budget allotments. Seldom does the Ministry of Finance allocate funds for specific bioengagement activities. (For example, see Appendix D.4 for a discussion of the activities of many institutes of the Siberian Branch of the Russian Academy of Sciences that have obtained funding for bioengagement.)

Russian officials and specialists have repeatedly emphasized the importance of orienting joint projects toward resolving day-to-day health, agriculture, and environmental concerns of the Russian government and the Russian population. However, a key U.S. concern in proposing bioengagement activities during the 1990s and early 2000s was the potential misuse of dangerous pathogens. At times, this mismatch of priorities of the funding entities in the two countries has caused complications in launching projects, but usually compromises have been reached.

Russian investigators have directed much of their attention to coordinated research approaches—with most of the research activities sited in Russia—that effectively use their experience and their laboratory capabilities in ways that will continue after conclusion of U.S. participation and support. U.S. counterparts have also been concerned about long-term maintenance of enhanced capabilities of Russian institutions. However, their overriding priority has usually been to complete cooperative projects that are undertaken and only then become concerned about continuation of the collaboration efforts.

In 2009, the presidents of Russia and the United States established the U.S.-Russia Bilateral Presidential Commission (BPC) as an important component of their commitment to reset the U.S.-Russia political relationship. (See Appendix E.1.) A number of BPC working groups have considered different aspects of bioengagement. While the commission focuses primarily on government-to-government programs, it recognizes that less formal institution-to-institution and scientist-to-scientist relationships within both the public and the private sectors are also important.

However, in 2012 the Russian government informed the United States that the Cooperative Threat Reduction Program administered by the U.S. Department of Defense (often referred to as the Nunn-Lugar Program) would not be extended in Russia beyond 2013. Also, the Russian government advised the U.S. Agency for International Development that it should close its offices in Moscow. One year earlier the Russian government had announced that in 2015 it would withdraw from the agreement and the associated protocol that established the International Science and Technology Center (ISTC) when all projects in Russia will have been completed. For almost two decades these three programs have provided hundreds of millions of dollars for bioengagement activities. Indeed, they have been important pillars of bioengagement for many years. As a result of the Russian actions, future cooperation in the life sciences will differ significantly from past activities.

NEW PRIORITIES IN INTERNATIONAL COOPERATION

For the past several years, Russia has been reorganizing its science, education, and innovation systems against a background of economic uncertainty. A consensus seems to have emerged within the Russian government that modernization of Russia depends in large measure on engagement with the international community. Despite the major changes in the intergovernmental bilateral relationship noted above, the United States remains high on the government's list of countries with relevant experiences and successes.

An important Russian government goal is for many universities and scientific institutions of the nation to gain recognition as equal to counterparts in other industrialized countries. At present, few Russian universities are on the short lists of leading educational institutions of the world. Thus, at times they have difficulties attracting attention of the world's top scientists, whatever the Russian achievements.

It has not been easy for the government or the population of Russia to change systems that have been in place in Russia for decades. Vested interests and well-developed procedures to control international relationships have often been barriers to new approaches. To help improve an integrated scientific infrastructure that links with the international scientific community, the Russian government has promoted the following approaches during the past several years.

- Designation of 29 elite universities as "research universities," with special funding, to advance integration of research and education while expanding international outreach to leading scientists throughout the world. A few of these universities have well-established strengths in the biological sciences.
- Provision of "megagrants" (equivalent to $5 million for each grant) to 79 Russian university departments selected on a competitive basis to attract world leaders of science to work at least 4 months annually in Russia for 3 years, where they are to establish and lead laboratory teams. Several American biologists were included in the teams to be supported by the initial 79 awards, with more awards scheduled.
- Support for small Russian technology-oriented businesses to work with universities in promoting technology transfer, with special advisory services provided at times by American and other international specialists.
- Establishment of a new high-technology flagship university near Moscow, named Skolkovo Institute of Science and Technology, which is to incorporate experiences of the Massachusetts Institute of Technology within its graduate education and research programs, with affiliated research centers located throughout the country, and indeed around the world. (See Appendix E.4.)
- Financial support of the Skolkovo Foundation and Rusnano in Moscow that are explicitly targeted on linking Russian scientific capabilities with commercial interests in the biomedical field and in the following four other priority fields: nuclear, space, energy, and information technologies. (See Appendixes E.3 and E.5.)
- Establishment of government-supported venture capital funds, with investments in biotech companies on the priority list.
- Federal requirements for state-owned strategic industrial companies to devote a significant percentage of sales to support research and development, including support of technology development activities at Skolkovo where, as noted above, biomedicine is one of the priority fields of interest.
- Designation of and financial support for the Kurchatov Institute of Atomic Energy as the nation's first independent national research center, with the institute expanding its capabilities in nanobiology research.

U.S. government financial capabilities for supporting bioengagement have been decreasing as collaborative programs are completed and resources are diverted to other deserving programs. Russia's capabilities to finance cooperative activities are steadily increasing. But still, the Russian financial contributions to cover direct expenses of current cooperation in the biological sciences lag behind U.S. contributions.

As to industrial interests, investments in Russia by U.S. pharmaceutical and biotechnology companies have remained at a low level, due in large measure to questions as to the business climate in Russia. Few Russian companies are currently in financial or technical positions to risk investments in international cooperation as an important component of their business strategies. Russian government venture-capital investments in biomedical activities in the United States that are then linked back to activities in Russia are in their formative stages and reflect a lack of confidence in the capabilities of Russian companies to move forward on their own. Many biology-oriented companies in both countries maintain a watch-and-wait policy before investing in manufacturing activities across the ocean, while progress toward a well-functioning market economy in Russia moves forward only slowly.

SCOPE OF THE STUDY

The committee focused primarily on *bilateral* activities involving important government and nongovernment institutions in the two countries. The committee recognized the significance of multilateral activities, and particularly programs of international organizations such as the United Nations Educational, Scientific, and Cultural Organization; United Nations Environment Program; World Health Organization; World Organization for Animal Health; and Food and Agriculture Organization. But assessments of the many multilateral activities that have been carried out would have greatly expanded the scope of the study and therefore were not undertaken, with one exception.

The report does address U.S.-Russian biology-oriented activities that have been financed in large measure by the United States and facilitated by the ISTC, which has its headquarters in Moscow. (See Appendix E.2.) This international organization has played a unique role in supporting cooperation linked to proliferation concerns that has engaged Russian and American scientists, as well as assisting with activities involving other countries from Europe and Asia and from other states that emerged from the former Soviet Union.

However, the Russian government has taken the position that the era of redirection of underemployed defense scientists to civilian tasks, which has been the principal role of the ISTC, has been completed. Therefore, the government considers that there is no longer a need in Russia for the ISTC. But the committee responsible for this report believes that the accumulated experience of the ISTC deserves careful attention, within Russia and globally.

Bilateral cooperation in space exploration has long had unique political support within the governments and among the general populations of Russia and the United States. The direct and indirect costs of the large manned spaceflight programs have been shared by the two countries. This report briefly mentions a few bilateral research projects in space biology that are of special interest to the international scientific community. However, a review of the overall effort in the life sciences to ensure the well-being of astronauts and cosmonauts in space is beyond the scope of this effort.

Finally, a comprehensive assessment of bilateral cooperation in many other aspects of the life sciences over 15 years is not possible because of the large volume of activities. The committee addressed limited but important portions of many relevant bilateral programs—including both past and current programs. In selecting activities for consideration, the committee gave special attention to bilateral efforts that (a) have received high levels of financial support from the two governments and from the private sector; (b) have resulted in significant impacts of security, scientific, and economic importance; (c) have encountered substantial problems and provide lessons learned for future programs; (d) hold considerable promise of important achievements of mutual interest through effective integration of U.S. and Russian scientific capabilities in the decade ahead; and/or (e) represent a broad spectrum of various types of programs that have been carried out.

The committee gave priority to looking to the future. Many of its judgments have been based on past experiences that retain their relevance for successful engagement, and particularly engagement that continues for many years. Other comments as to future challenges reflect the dynamic developments in the biological sciences and biotechnology throughout the world.

LEVEL OF INVESTMENT IN BILATERAL COOPERATION IN THE LIFE SCIENCES

Over 15 years, investments of the two governments and, to a lesser extent, private-sector companies and institutions in the two countries in bilateral cooperation have been extensive. The committee estimates that at the peak of the cooperative activities during the beginning of the 2000s, the total expenditures by the two countries—covering both direct and indirect costs of bioengagement—exceeded the equivalent of $150 million per year. By 2011, this investment had decreased to about $25 million per year. The total expenditures since 1997 were considerably more than $1 billion. Some fragmentary data concerning expenditures is included in the appendixes to this report. These data have been helpful in estimating some costs.

A more accurate accounting of the levels of expenditures has not been possible for the following reasons.

1. Few, if any, government agencies in either country have readily available records of expenditures for bioengagement—even expenditures to cover direct costs—going back 15 years. Many have difficulty assembling authoritative data for 2011. For example, the National Institutes of Health grants program is one of the best documented activities. However, available data do not include all of

the matching contributions by Russian institutions or costs of administering the grants program.

2. Few agencies break out budgets for the life sciences. Indeed, the breadth of the life sciences is often underestimated, given the increasing convergence of chemistry, physics, mathematics, and material sciences with biology.

3. Agencies sometimes have budgets for international activities but do not break out biology-related aspects of international activities, nor do they separate proposed budgets for U.S.-Russian engagement as distinct from activities involving other countries as well.

4. When accounting for costs of international programs, agencies seldom include the costs incurred by government employees who oversee specific international programs on a full-time or part-time basis.

5. Many projects rely to a considerable extent on matching contributions by host institutions, and these costs are simply absorbed by the host institutions as overhead. (See, for example, Box I-1.) In some cases, the financial contributions of host institutions have exceeded external grants directed to the same projects by a factor of 10.

6. U.S. contracts and grants awarded to Russian institutions or individuals do not include indirect costs as discussed above.

7. Excellent statistics are maintained by the ISTC, but even they do not include matching costs by Russian institutions, indirect costs, or the funds provided to the U.S. collaborators for their participation.

Box I-1
Costs of Collaboration Absorbed by Russian State Research Center Vector

Because of the need to fulfill international grant commitments, Vector, for example, (a) tripled its energy and water consumption at its own expense for a few years, (b) spent additional funds on materials and reagents, (c) purchased personal protection equipment, (d) redirected internal funds to support engineering personnel, and (e) provided funding for joint publications after grant funding had been expended.

SOURCE: Former Scientific Leader of Vector, June 2012.

STRUCTURE OF THE REPORT

Four dimensions of bioengagement that provide the framework for the report are (1) enhancement of security, (2) advancement of science, (3) applications of scientific findings, and (4) contributions of science in addressing problems of global and regional interest. The objectives of engagement in these four overlapping areas include the following:

1. **Improve security** by helping to (a) reduce the risk of proliferation of potentially dangerous biological agents and expertise in the two countries to irresponsible governments or to groups with hostile intentions and (b) prevent bioterrorism, at home and in other countries strengthening response capabilities should bioterrorism attacks occur.
2. **Increase U.S. and Russian contributions to the advancement of science,** and particularly to improvement of the knowledge base for understanding fundamental scientific issues.
3. **Develop programs that apply existing scientific capabilities to address public health, agricultural, and environmental issues,** including (a) utilization of the results of research and (b) contributions in responding to the needs of the general populations for better and cheaper products, technical information, and specialized services that are developed or provided by governments.
4. **Contribute to resolving global and regional issues,** wherein understanding the biological dimensions is critical in developing appropriate approaches by the two countries and the international scientific community more broadly.

The report begins with a discussion of the importance of bioengagement. After considering examples of activities related to each of the four objectives set forth above, the report addresses positive impacts and shortcomings of activities. It then considers impediments to cooperation and lessons learned during bilateral cooperation in recent years. An important chapter is devoted to the strategic, financial, and organizational aspects of bioengagement, with special attention devoted to sustaining existing programs that have high payoffs while developing a new approach to deepening involvement of the best scientists in the two countries in collaborative efforts. The report concludes with a presentation of three major recommendations of the committee that reflect the importance of bioengagement in general, and strengthened international networks of researchers in particular, in the years ahead.

A number of appendixes are included in the report. They discuss the interests and activities of U.S. and Russian sponsors of bioengagement, the types of cooperation supported by a number of Russian institutions, and examples of bioengagement programs that have been successful. They underscore the broad reach of bioengagement and help set the stage for consideration of future activities.

CONSULTATIONS AND RELATED REPORTS

In preparing this report, committee members and staff carried out consultations with many dozens of organizations and individuals in Russia and the United States concerning their experiences in designing and implementing past bilateral programs. Of comparable importance were their visions of future approaches and of methods for improving program implementation. These organizations and individuals have been particularly helpful in providing details that are included in the events highlighted throughout the report. A few specialists from other countries were also consulted. Appendix A.3 identifies some of the key organizations that provided information to the committee during preparation of this report.

During the late 1990s and the 2000s, the National Academies prepared a number of reports on U.S.-Russian scientific relations in general, and cooperation in the life sciences in particular. These reports are identified in Appendix A.2. Many other relevant observations are included in books of well-qualified observers, compendiums of activities prepared by other organizations, international journals, and news outlets. A few of these sources that were of particular help in preparing this report are also identified in Appendix A.2. Unfortunately, there have been very few authoritative publications prepared jointly by U.S. and Russian organizations or authors, which have focused explicitly on U.S.-Russian bilateral engagement, and particularly on the future of this relationship in the biological sciences. This report should assist in filling that gap.

That said, the most important source of information for the report has been the observations of the committee members themselves, who have personally observed development and implementation of many aspects of bioengagement during recent years.

1

Importance of U.S.-Russian Bioengagement

Government pronouncements in Moscow, Washington, and other capitals about the remarkable advances in the biological sciences and biotechnology increasingly underscore the scientific, economic, health, and environmental importance, as well as the security significance, of these achievements.[1] Meanwhile, the U.S.-Russia Bilateral Presidential Commission (BPC) that was established in 2009 continues to signal endorsement by both governments of joint science and technology efforts in areas of common interest. As of September 2012, 6 of the BPC's 22 working groups had interests in engagement in different aspects of the life sciences.[2]

Major issues addressed in this report include the types and levels of support that the governments have provided to take advantage of important opportunities for mutually beneficial bioengagement. Anticipated budget reductions throughout the U.S. government will likely constrain new initiatives. In recent years, the Russian government has established a number of outreach programs within elite universities, the Skolkovo Foundation, Rusnano, and other organizations, as discussed in the Introduction. Financial support for these initiatives by the Russian government will most likely continue, although the announced levels of governmental support may not be reached. At the same time, the level of fulfillment of the often-stated commitments of the two governments to share the direct costs of many types of bioengagement is uncertain.

Against this background, the arguments for reversing the decline of financial support for U.S.-Russian bioengagement during the past several years are presented throughout this report. The list of benefits to both countries from a robust bioengagement relationship has been extensive. And many successful early programs were to be only "stage setters" for expansion of bioengagement activities.

Revitalization of collaborative efforts can benefit from more sophisticated research, diagnostic, and remediation tools that are now available. The governments have drawn on important experience for more-effective synchronization of parallel activities, such as disease surveillance activities of global interest. At the same time, cumbersome approaches of the past for developing and managing joint efforts can be replaced by streamlined efforts that reduce impediments to cooperation and increase opportunities for positive impacts.

This chapter provides a broad overview of the unique opportunities for obtaining higher returns on investments in bioengagement. The discussion addresses special attributes of the U.S.-Russian relationship that can continue to lead to significant scientific results, while underscoring the importance of government financing to initiate long-term programs. Many examples of specific activities that have led to mutual benefits during the past decade along with suggestions for new approaches are then presented in subsequent chapters.

IMPORTANT CHARACTERISTICS OF THE U.S.-RUSSIA RELATIONSHIP

Extensive Scientific Capabilities of the United States and Russia

Many tens of thousands of scientists and members of their support staffs in both the United States and Russia, with ages ranging from the early twenties to the eighties, are engaged in (a) carrying out research activities in a number of subfields of biology and (b) promoting applications of biological and biotechnology advances at home and abroad. Skilled scientists in the two countries account for an estimated 20 percent of the world's highly trained specialists involved in activities linked to the life sciences.[3] Of course, with the rapid growth of the high-skill labor pools in India and China, the percentage will decline. However, for the next decade, the number of experienced life scientists and skilled young investigators in the two countries will continue to be a significant portion of worldwide capabilities.

Reflecting the importance of the life sciences, a large percentage of the global scientific work force, including both researchers and service providers, is involved in advancing the biological sciences and biotechnology. They assist in protecting human health, increasing the food supply, developing new energy sources, and enhancing the quality of the environment. The intensity of international interest in advances in the biological sciences and biotechnology, which address the very basis of life, continues to rise. At the same time, many countries are becoming more deeply immersed than ever before in interdisciplinary approaches that attract increased attention of specialists in a variety of fields, which intersect with biology—e.g., physics, chemistry, mathematics, computer science, engineering, and bioinformatics. Adequate recognition of this convergence of various disciplines is important for designing and carrying out research in both countries, and particularly in Russia. There, the physical sciences have for decades been the greatest strengths of the scientific enterprise, but too often they have been somewhat isolated from important biological research efforts.

In addition to the communities of well-established specialists in biology who will continue their careers in the United States and Russia during the next decade, the number of temporary scientific workers and of advanced students from abroad at U.S. universities, and to a lesser but still significant extent at Russian research centers, is growing. In short, the total efforts focused on moving forward the frontiers of the life sciences in the two countries are extensive. During the next decade, only a handful of countries will have the large number and diversity of biology-oriented scientific institutions that can rival the capabilities of institutions located either in the United States or in Russia.

In Soviet times, both the United States and Russia devoted significant resources to many areas of the biological sciences that were of international interest. The United States was among the world's leaders in achieving scientific breakthroughs as the nation expanded its portfolios of science-intensive activities. But for decades, the USSR was recovering from the Lysenko era of the late 1940s, when his theory of "inheritance of acquired characteristics" had for a short time become the official dogma.[4] Thus, it is not surprising that for many years the scientific productivity of American researchers and the number of articles published in international journals with roots in the United States were much stronger than productivity and publications in the USSR.

The publications gap has continued in recent years, further aggravated by a brain drain of some of the most productive young Russian scientists, including a significant number who have moved to the United States.[5] The gap, in large measure, reflects the inadequate number of active Russian investigators currently in the 40–50 age group. Thus, in the near term, Russian science will gain substantially from bilateral cooperation that provides access to a broader range of specialists.

While the overall number of researchers in Russia has stabilized, as indicated in Appendix F.2, the impact of the brain drain is best measured by the quality rather than the quantity of the scientists who have left Russian laboratories. According to a number of Russian laboratory leaders, far too many of the best young researchers have departed for positions in the United States and Europe. However, opportunities for Russia to participate in international projects that involve recognized scientific leaders from abroad has at times been an effective way to encourage outstanding investigators to return to or to remain in Russia.

American researchers also benefit from cooperation. Those who do not regularly scrutinize Russian-language journals and have not been able to assess in detail the scientific methods used in Russia are given the opportunity to fill in many gaps in their understanding of Russian achievements through scientist-to-scientist contacts. In short, while the United States has been the international leader in the biological sciences, Russia has been an action-oriented follower, although some of its achievements have been overlooked by the international community. Unfortunately, the Soviet-era legacy of not involving in joint activities many important Russian specialists who had been isolated from the mainstream of international science still remains in a number of topical areas.

An exception to U.S. dominance in significant scientific fields has been the extensive investigations of dangerous biological pathogens within the Soviet defense sector during the 1970s and 1980s. In this period, the USSR mounted large and unique programs to explore the capabilities of biological pathogens that might be produced in large quantities. At the end of the 1960s, the United States reduced the size and scope of its defense-related research in compliance with the Biological and Toxin Weapons Convention (BTWC), which would soon enter into force. Then in the early 1990s, Russia abandoned inappropriate research efforts as it announced its commitment to the BTWC as well.

From the earliest days of defense-oriented research, many potential spin-off benefits for civilian science became apparent to scientists in both countries. It was obvious to them that scientists could and should improve understanding of the characteristics of diseases caused by exposure to dangerous pathogens that occurred in nature or could be manipulated in laboratories for destructive purposes. Among the pathogens of interest were those that caused plague, hemorrhagic fevers, and anthrax, which were encountered naturally in some areas of both the United States and Russia.[6]

The Russian workforce suffered severe reductions in both quantity and quality of its research and application efforts during the economic crises of the 1990s. Brain drain, equipment obsolescence, loss of respect for science, and low priority for research in Russia took a huge toll in reducing the productivity of the research community. But the country is now slowly returning to a prominent position in a few areas, and U.S.-Russian bioengagement has been a significant factor in this recovery.[7]

Looking ahead to the next decade, the history of a strong Russian system of higher education, developed largely in the Soviet era, then weakened by the economic crisis of the 1990s, and now supplemented with an increasing emphasis on university-based research, will continue to be of considerable importance. While these universities are becoming stronger, few have kept pace with leading universities in many other countries. The Russian government is expecting substantial payoffs from its large investments in both universities and other research centers as well as in applied biotechnology activities. However, biotechnology hubs should be effectively linked to the research and educational establishment if Russian investors and investigators alike are to work successfully on the frontiers of biotechnology.

As to the size and strength of the scientific workforce in the many fields related to biology (such as agriculture, health, environment, pharmacy, veterinary science, and bioengineering disciplines), the Russian commitment to producing well-trained specialists in the foreseeable future seems clear. Many industrialized countries will increase their investments and the number of participants in their research programs. However, Russia plays an important and sometimes a unique role in some niche areas of biology of general interest to the global community, including the United States.

The Cold War Legacy

For the next few years and probably longer, the experiences during the cold war will at times continue to have a chilling impact on the U.S.-Russian relationship in a number of areas, particularly in fields that encompass technologies that can be misused by malcontents for hostile purposes. The deep roots and expansive dimensions of this sensitive bilateral relationship are unique in the world. Significant progress in developing mutual trust and respect concerning intent and activities of the two governments and particularly within their highly skilled workforces has been repeatedly recorded in recent years. But suspicions about past and present intentions have not completely disappeared in Washington or in Moscow. A strong bilateral relationship in biological research and biotechnology that rests on transparency and activities of mutual interest has been and can continue to be critical in preventing miscalculations or dangerous scenarios by either side or by third countries that have access to U.S. or Russian expertise. An increased focus on bioethics, which is currently gaining international attention, by both parties would be helpful in this regard.

As noted earlier, the productive interactions involving highly accomplished scientists who had worked on defense-oriented programs in the two countries have declined since the early 2000s. This reduction of collaborative activities has at times raised questions as to whether the early initiation of joint programs was based primarily on mutual interests in advancing science or was motivated primarily by efforts to simply obtain information on past and current activities of former enemies with uncertain future agendas. While both objectives were probably important, the primacy of contributions to advance science rather than to collect information needs to be continually emphasized. The approaches adopted in joint U.S.-Russian research programs to investigate the characteristics of dangerous biological pathogens might be considered as a standard that could be applied more widely beyond the two countries. (See, for example, Appendixes C.2, C.3, and C.4 concerning successfully conducted joint research projects involving many types of technologies, including some of particular concern.)

Geography and Ecological Diversity of the Two Countries

Russia occupies about one-eighth of the land surface of the world, spanning thousands of miles. The United States encompasses a land area about 60 percent the size of the surface of Russia. Together they occupy 34 percent of the land mass of the northern hemisphere, with many shared ecosystems and species. Each of the countries has vast experiences in investigating living organisms under a variety of climatic conditions—from human populations currently surviving and indeed thriving in harsh environments to microbes of historical interest. Their diverse resources have been the subject of many common studies by scientists of the two countries.

Aquatic and wetland systems are of considerable interest in both countries, and indeed on a global basis as well. The characteristics of these systems and their maintenance in a changing climate are particularly significant in drought or flood conditions. The vegetation in both countries is of importance as a carbon sink, as are the large carbon-laden deposits of resources that underlie the forests and other vegetation of the northern reaches of the world.

Both countries routinely collect extensive information from their sensors on satellites, as well as data from field expeditions, about ecological resources of potential interest to both countries. Russia has records of research and scientific applications under conditions not encountered in the United States, but of sufficient similarity to warrant interest of American biological scientists. For example, Russian data on fishery resources in the oceans are important in ensuring survival of certain species, but are not always fully utilized. At the same time, U.S. analyses of vast amounts of data through satellite, aerial, and ground explorations concerning the natural environment on several continents, which in some regions have similarities to conditions encountered in Russia, has been of considerable interest to Russian scientists.

In summary, the case for working together in different geographical environments to gather missing data concerning complex living systems under different, but related, conditions seems clear.

Surveillance for Trends and Outbreaks of Human and Animal Diseases

Both the United States and Russia have well-developed disease surveillance systems for tracking trends and identifying outbreaks involving human and animal diseases in their respective countries. Also, both countries give considerable attention to trends and outbreaks throughout the world.

With regard to human health, the United States relies in large measure on surveillance activities that are responsibilities of the 50 states. The Centers for Disease Control and Prevention provides coordination and standards for the overall national effort. Russia has a national network of nearly 2,400 standardized surveillance stations of different levels of capabilities. The nation's activities are coordinated regionally and nationally by the Federal Service for Surveillance for Protection on Consumer Rights and Human Well-Being. Reports from field stations are processed and analyzed both in the regions and in Moscow.

During the past 15 years, the capabilities of U.S. disease surveillance systems have improved, with the introduction of advanced communication, analytical, and data processing systems that have led to better and more timely reporting at the local level. During most of this time period, the Russian systems suffered from financial cutbacks. Nevertheless, they continued to operate without many difficulties. They are now recovering from the temporary decline in capabilities due to obsolescence of equipment, continued use of outdated methodologies, and aging of the workforce.

In the agricultural field, the national governments in the two countries, with the support of nationwide networks of research centers and of inspectors in the field and at food-processing facilities across their countries, maintain surveillance to detect plant and animal diseases of concern. Both countries have extensive experience in consolidating and distributing reports from their internal systems. Internationally, they are interested in linking these internal systems with other networks of the international community through the World Organization for Animal Health and Food and Agriculture Organization.

The experience of the two countries in carrying out surveillance activities over large urban and rural areas is vast. In the years ahead, this experience can provide lessons learned for many other nations with different demographic situations, geographic terrains, and technical capabilities. In all countries, standardization of approaches that support international efforts is important, although limitations on financial, technical, and human resource capabilities often constrain near-term adoption of compatible approaches among countries. The combined experiences of the U.S. and Russian systems can at times be helpful to other nations aspiring to achieve reliable surveillance capabilities.

International Outreach of the Two Countries

In recent years, the United States and Russia have each conducted many types of cooperative bilateral programs in the biological sciences with dozens of countries throughout the world. While the United States has had more financial resources to devote to this outreach, Russia has maintained an important array of international programs; and its linkages with institutions in distant lands are now increasing. These programs have usually been embraced by individual institutions and specialists that maintain their contacts over the long term. Of course, availability of financial support and the possibility of professional rewards can be strong incentives for participation.

Often the interactions between Russian and American specialists working abroad on separate missions intersect, although Russia and the United States may be following different paths for cooperation with other countries. Russia has focused most of its cooperative programs abroad in the states that were components of the former Soviet Union. Collaboration with colleagues in India, China, Mongolia, Vietnam, Cuba, and other old and new partner countries continues to develop. Meanwhile, thousands of professionals in the United States have long-standing ties with colleagues throughout the countries of the Americas, the European Union, and East Asia—with its foreign assistance, disease surveillance, and health infrastructure programs extending the outreach into Africa and to middle- and low-income countries on other continents as well. As an example of unique aspects of this outreach, which is of considerable interest to Russian scientists, the United States is expanding its integrated surveillance of human and wildlife populations in developing countries, in anticipation of the emergence and spread of zoonotic diseases from animals to human population in and near urban areas.[8]

The international outreaches of the two governments, when aggregated, cover most areas of the world. Activities sponsored by international organizations and international companies also involve Russian and American specialists. In addition, important cross-boundary activities have been initiated by individual research and education institutions, with or without government support. They often are based on the interests of specialists who have developed professional and personal relationships with like-minded colleagues.

In summary, there are few areas of the world where the presence of Russian and/or American biology-oriented specialists—from doctors to engineers, from teachers to practitioners, and from researchers to entrepreneurs—has not become commonplace.

BENEFITS FROM BILATERAL COLLABORATION

Building on the background described above, a variety of benefits that would accrue from bilateral cooperation in the biological sciences between the United States and Russia during the next decade are set forth below. Examples of research topics that offer high promise as focal points for engagement are presented in Chapter 10. This forward look is based in large measure on experiences of the two countries in scientific cooperation during recent years, which are documented in Chapters 2, 3, 4, and 5, as well as in the appendixes.

Internal capabilities and international interests of both countries in biology-related activities will continue to grow. The opportunities for cooperative endeavors will increase. The major uncertainty, as previously noted, is the level of financial commitments that the governments are prepared to make to bilateral cooperation. Of course, these financial commitments are usually linked to the political relationship between the two countries. Also linked to financial commitments is long-term continuation of both large and small efforts that in time can fully demonstrate their value.

Benefits to the United States

The importance to the United States of a sound bilateral relationship with Russia has been regularly emphasized by senior American government officials, particularly since 2009, when the "reset" of the relationship was highlighted by the secretary of state.[9] Bioengagement has been one of the important aspects of this relationship.

As previously noted, Russia has a large number of experienced scientists, including both researchers and practitioners, often probing a variety of geographical areas to obtain insights on biological conditions and transformations affecting both the residents and the ecological resources that are unique to Russia but are also of interest to the international community. Russian institutions have extensive data banks of scientific interest that are difficult to access and to use efficiently without active collaborative projects. Also, a number of these institutions have traditions of innovative approaches both in the laboratory and in the field. But some of their successful methodological approaches are not well known internationally.

Russian institutions have developed considerable experience in analyzing a wide variety of organisms and ecosystems that are of interest to American investigators but have not been well studied in the United States. For example, Russia has extensive research experience in the fields of forestry, plant science, and soil science, giving particular attention to the characteristics of various ecological zones. Bilateral collaboration encompassing ecological considerations in Russia enables American researchers both (a) to witness firsthand the basis for Russian reports on these organisms and ecosystems and thereby be in better positions to judge the importance and authenticity of relevant Russian publications and (b) to recommend supplemental investigations that augment initial Russian findings, which are of particular importance in providing a global context for investigations of ecological phenomena in the United States.

Many Russian colleagues are interested in participating in bilateral cooperation, often at low costs to the Russian or U.S. financial sponsors of such cooperation. Once Russian investigators interact with American colleagues, they usually devote considerable time and effort to continuing mutually beneficial cooperation through adjustments of their personal research agendas. In general, Russian scientists are noted for being "all in" with joint U.S.-Russian undertakings.

In applied technologies, Russia is likely to be a growing future market for U.S. biotechnology products as the Russian economy continues to develop, with demands for a wider variety of high-technology medical and agricultural products. The quality of imported drugs, vaccines, and diagnostic systems into Russia from some countries—particularly developing countries where corruption is of concern—has long been questioned by both Russian officials and the general population. Products of well-known U.S. pharmaceutical companies have usually commanded greater respect, particularly products with complicated vaccine and drug formulations. As potential opportunities for profitable U.S.-Russian joint ventures and other types of international investments increase, the reputation of U.S. achievements in biotechnology will continue to command considerable attention within Russia.

Bilateral cooperation that is endorsed by the two governments should continue to open otherwise closed doors in Russia. Thus, it is important for security as well as for scientific reasons for U.S. institutions to be engaged in cooperative research and related field activities in Russia. The alternative is to sit on the sidelines speculating on developments within Russia. Such long-distance impressions can result in false alarms within the United States in reacting to uncertain allegations of disease outbreaks, misinterpretations of Russian technical objectives, lack of awareness of existing Russian data that are available, and administrative difficulties in organizing ad hoc visits to obtain snapshot impressions of the quality of activities in research institutes that were once recognized as international leaders.

As previously noted, Russian scientists do not publish in English-language journals as extensively as scientists of the United States and many other countries. Cooperation often leads to publications, documenting Russian past and current achievements. American scientists can help Russian colleagues overcome their lack of experience in dealing with western publishers and their difficulties in handling the English language. An increase in such publications will provide American researchers with easier access to Russian data that might otherwise remain in inaccessible libraries. (See Appendix F.1 concerning the relatively small number of jointly authored articles involving Russian coauthors in peer-reviewed journals and related publications.)

Benefits for Russia

Many of the world's leading biomedical laboratories are in the United States. They offer a variety of opportunities for visiting Russian scientists to improve their insights as to recent research achievements in the life sciences. Russian scientific visitors may have opportunities to assess methodological approaches that are appropriate for their laboratories in Russia as well. Also, U.S. laboratories are usually well connected internationally with contacts of possible interest to Russian colleagues.

Many U.S. universities have become magnets for attracting outstanding research-oriented students from throughout the world, including Russia. Contacts that develop among important counterparts from many countries visiting U.S. universities during the early stages of their careers are often beneficial for visiting Russian specialists in both the short and long terms.

Overall, U.S. laboratories are better equipped with modern instrumentation than Russian laboratories. Exposure of Russian specialists to advanced instrumentation may at times help their laboratories make wise investment decisions in choosing equipment that is most cost-effective for their needs. Also, bilateral cooperation can provide training opportunities for Russian specialists to become familiar with equipment operations, thereby reducing costs in Russia in bringing new equipment online. Russian exposure to equipment in other countries will also be useful, but there will be lingering questions among some Russian specialists as to whether they have seen the best, which is often equated with the state of the art in the United States.

The United States is a world leader in agriculture research, including approaches to reduce animal and plant diseases and increase agricultural productivity—topics that are of particular interest in Russia. Countries other than the United States also have strong agricultural research activities. However, the breadth of experience available in the United States often provides more complete coverage of areas of priority concern to Russia than experience of other countries. Recent bioengagement in this area has been beneficial for both countries, as discussed in Chapter 4. This cooperation provides a basis for future efforts.

The United States has more experience than Russia in the introduction of genetically modified (GM) crops into large-scale production. If the Russian government increases its interest in encouraging developments in this field, the approaches of the United States to evaluate food safety and to limit environmental effects can be helpful to both Russian scientists and regulators. Important Russian scientists are particularly hopeful that the positive U.S. experiences will counter some of the misleading European commentary about GM organisms. Many protocols for carrying out both research activities and for introducing new GM crops into production have been well developed and adopted in the United States, and they can provide models for Russian approaches.[10]

The U.S. government and indeed many of the nation's scientists active in biological research and biotechnology have embraced the concept of **responsible research in the life sciences.** Exchanges can help Russian scientists join the international dialogues on this topic. Also, bioengagement can quickly lead to new insights about recent international developments concerning the handling of pathogens that should help avoid missteps in Russia.

Finally, for many Russian scientists, one of the most important aspects of engagement is the opportunity to upgrade skills in research management. The transition from Soviet-style management to western-style management has not been easy. Twenty-two years after the splintering of the Soviet Union, Russian researchers and their mentors in the universities and at research institutes are still in the early stages of mastering new management skills. These personal capabilities need to be compatible with decentralized planning and free market economies while taking into account traditions and practices in Russia. In short, research planning, execution, and evaluation often improve during joint activities.

Benefits for Both Countries

Investigations of outbreaks of contagious diseases are a priority activity in both countries. The likelihood of major scientific advances in addressing widespread concerns will be increased through coordination of parallel efforts of the two countries, as an important component of the broader international effort. A bilateral commitment to sustain these parallel efforts and share their results over the long term can improve the prospects for important advances.

Of particular importance are activities of outstanding young scientists and entrepreneurs in the two countries and opportunities for international outreach. Both governments recognize that the technological futures of their countries are increasingly in the hands of new generations of scientists and are giving them special incentives to become leaders of initiatives of the government, such as priority for involvement in the laboratories at Skolkovo. At the same time, the U.S. scientific community continues to rely on the unbounded energy and ideas of fresh graduates of leading U.S. universities to find new trails through the challenges of biotechnology at home and abroad. Of course, continued involvement in joint activities of experienced managers, scientists, and other specialists, who are recognized leaders in their fields, is important. But the preparation of their successors for international leadership roles is of comparable importance.

Turning to biosecurity in the broadest sense, there are opportunities to strengthen and build on bilateral foundations that have been put in place during the past two decades. Now there is widespread concern that past achievements may atrophy with the changing status of the International Science and Technology Center (ISTC) and the declining budgets in the United States for support of Russian-oriented programs. New bilateral mechanisms to carry on the work initiated through the ISTC can increase the likelihood that momentum in gaining common understanding on biosecurity issues throughout the states of the former Soviet Union will not decline significantly. The roles of the United States and Russia will be at the center of the debates over successor mechanisms for cooperation to the ISTC. While these discussions will continue to be multilateral efforts, common U.S.-Russian views will be important in determining the outcomes of preliminary consultations that are under way.

The United States and Russia have the deepest histories in the world in dealing with extremely potent pathogens, and their experiences provide a strong basis for partnerships. The degree to which they cooperate directly will have a profound influence on the international community's attitudes and actions concerning the handling of pathogens and associated technologies that, if misused, can lead to catastrophes.

Bilateral cooperation between two countries that have been at the center of heated international debates over biosecurity obligations of state parties to the BTWC is important in overcoming the weaknesses of the BTWC. As the international community searches for acceptable procedures for compliance with the BTWC and related UN resolutions, U.S.-Russian collaborative efforts can continue to play a catalytic role in crystallizing common interests.

Through bilateral cooperation, the two countries can effectively contribute to the broad international agenda for addressing biosafety issues. These issues include, for example, (a) routine handling of dangerous pathogens; (b) responses to unanticipated health and safety problems that can arise when handling pathogens; (c) the need, criteria, and guidelines for establishing and operating high-containment facilities; and (d) coping with accidents involving a wide range of dangerous pathogens.

With or without bilateral cooperation, the two countries are viewed as pathfinders in many aspects of biosafety. The stakes are large, as the safety of people is on the line. Thus, it is better for the two countries to be working together and exchanging experiences in this regard than working along uncoordinated separate paths. Bioengagement can help ensure that this is the case.

The two countries have different sets of international contacts that open doors between counterparts and collectively provide excellent global coverage of almost all important research that could lead to significant discoveries in the biological sciences. Many developing countries have very few scientists who can address rapidly the emergence of new biology-oriented issues. For them to be able to simultaneously draw on U.S. and Russian mentors can avoid waste of time and money and reduce international misunderstandings and confusion.

In summary, historical reasons account for the different paths of the two countries in exploring many aspects of the phenomena encountered in the life sciences. They have established different priorities and developed different capabilities; but their common interests are magnified as both countries uncover new phenomena and attempt to assess the long-term impacts on health, agriculture, and the environment. Cooperation in understanding scientific discoveries, giving due consideration to both historical insights and biases, can increasingly benefit scientists and policy officials in the two countries.

Whether Russia's new innovation complex at Skolkovo, for example, meets its biomedical goals or falls short, the energy and resources of leading U.S. and Russian officials and investors devoted to this high-profile undertaking will probably be substantial. It is better for respected U.S. and Russian scientists to be jointly involved in assessing the potential benefits of devoting efforts to this route of cooperation, which seems to have assured financial support from the Russian government, than simply to speculate about the biomedical activities that are carried out or should be carried out by others. While the short-term payoff from such cooperation may be difficult to measure, collaborating scientists will be able to provide insightful perspectives that might not be otherwise raised in discussions of this important development. In doing so, important personal and organizational relationships will emerge.

CONCLUSIONS

The foregoing snapshots of some of the benefits from bilateral cooperation—benefits that have already been observed and additional benefits that are anticipated—lead to the following conclusions:

1. *In recent years, bioengagement activities have been undervalued in Washington and Moscow, as reflected in the steady decline in financial support in Washington for joint activities and the reluctance in Moscow to meet commitments to cover one-half of the direct costs of bioengagement.*

Common interests in the characteristics of large geographical areas, common commitments to pursue responsible science, and unrivaled experience in jointly addressing some of the most challenging biological developments in recent decades provide a strong basis for collaborative efforts of the future. Both countries have invested heavily in changing cold-war hostilities in the biological sciences into productive relationships that have involved thousands of specialists and hundreds of institutions. Now is the time to capitalize on the vast networks of personal and institutional relationships. It is not the time to walk away from investments that provide a unique foundation for future achievements that will benefit the two governments, the populations of the two countries, and the global scientific community.

The positive impacts of bioengagement activities in many areas of security, education, the economies, and the social lives of the two countries have been extensive. Indeed, many new dimensions have been added to the U.S.-Russian political and economic relationship through such engagement activities. Continuation of successful programs and initiation of new activities are in order.

The number of activities need not rival past numbers. But they should be at a level that will continue to provide continuing access by specialists of both countries to highly relevant activities in the other country. Joint programs should provide opportunities for laboratory, field, and academic partnerships in both countries.

2 *Individual investigators with appropriate skills who are prepared to pursue cooperative activities over the long term greatly increase the likelihood that cooperative activities will pay off for both countries.*

While past engagement activities have been organized largely on the basis of interests of institutions in the two countries, the most successful projects have usually relied heavily on individual scientific leaders who have taken responsibility for ensuring successful outcomes of complicated programs. These leaders should be selected with care. Among the primary selection criteria should be technical and managerial capabilities, skills in relationship building, and commitments to continue efforts for extended periods of time.

3. *Exceptionally well-qualified scientists, who are conducting research and related activities during the early stages of their careers and therefore are in positions to effectively promote continuation of international programs, should have greater opportunities to participate in important bioengagement activities sponsored by the two governments.*

The future leaders of science can bring new ideas and new vitality to bioengagement. They can help ensure that cooperation looks to advancing technological opportunities and is not frozen by nostalgia for outmoded methodologies of the past. Also, their involvement will provide a strong foundation for developing approaches that have high probability for being continued over the long term.

Special programs for young investigators may be necessary, given the frequent propensity of older scientists to dominate international activities of both countries. Consideration of jointly organized summer camps and meetings devoted to the frontiers of science in various subsets of biology seems warranted. Also, establishing special quotas for young investigators who apply for competitive international programs may be appropriate. A particularly noteworthy development has been the agreement between the Russian Ministry of Education and Science and the U.S. Department of Education calling for exchanges of a limited number of outstanding university science students. While there have been thousands of student exchanges that have touched the life sciences, this is the first time that the importance of exchanges of science students have been formally recognized in an agreement by the two governments.

In addition to reaching the foregoing conclusions, this chapter has set the stage for discussion of other conclusions in the chapters that follow.

NOTES

1. The plans of the U.S. and Russian governments to promote biotechnology, for example, are set forth in the White House, *National Bioeconomy Blueprint*, April 26, 2012, http://www.whitehouse.gov/blog/2012/04/26/national-bioeconomy-blueprint-released and Decree of the Chairman of the Russian Government, *Complex Program, Development of Biotechnology in the Russian Federation until 2020,* No. 1853P-P8, April 24, 2012, http://s3.amazonaws.com/zanran_storage/www2.foi.se/ContentPages/115876758.pdf.
2. Appendix E.1 summarizes some of the relevant interests of the BPC.
3. Estimate is based on data provided by the Higher School of Economics (HSE), Moscow, May 2012. See, for example, HSE, *Science Indicators: 2012,* p. 48.
4. David Joravsky, *The Lysenko Affair*, University of Chicago Press, 1986.
5. Op. cit., *Science Indicators*, pp. 372–375.
6. Committee members have had many discussions over the years with experts from both countries concerning the intersections of civilian and defense research interests.
7. National Research Council, *Biological Science and Biotechnology in Russia, Controlling Diseases and Enhancing Security*, Washington, D.C.: National Academies Press, 2006.
8. Stephen A. Morse, "Public Health Surveillance and Infectious Disease Detection," *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science*, Volume 10, Number 1, 2012.
9. In a speech at the Eurasia Foundation in Washington, D.C., in May 2012, Deputy Secretary of State William Burns described this relationship as follows: "Few regions matter more to our success and security than Russia and the other independent nations that emerged from the break-up of the Soviet Union…. Home to a quarter of a billion people, the countries of the region hold vast hydrocarbon reserves and pipelines critical to a secure global supply of energy. Beyond its oil and gas riches, Russia remains an influential player on the world stage…. It remains deeply in the interest of the United States to see a strong Russia continue to re-emerge, a prosperous and modernizing Russia fully integrated into the global economy, a Russia which makes it possible for their citizens to realize their extraordinary potential.… We cannot afford to be detached observers."
10. See Appendix F.4 concerning a U.S.-Russian assessment of the scientific basis for regulating GMOs.

2

Ensuring Appropriate Use of Biological Assets

Beginning in the late-1990s, for more than a decade joint projects that addressed appropriate use of biological assets dominated much of the bioengagement agenda.

This early impetus for addressing security concerns was driven primarily by the U.S. government. At that time the Russian economy was in a state of free fall, with resources available from the Russian governmental or nongovernmental sectors for scientific activities being very limited. While the Russian government was hesitant at first to participate in cooperative activities designed primarily to contain sensitive technologies, the Russian scientific workforce was desperate for financial relief. The government soon became interested in cooperation in biosecurity, provided there were also opportunities for advancing its scientific agendas. But Russian ministries simply did not have funds to make major contributions to joint activities.

At times, Russian scientists were able to use limited funds available at the institution level to support cooperation. More often, they relied on U.S. financial support while contributing some labor and supporting services without compensation to joint efforts, as discussed in the Introduction to this report. In any event, the program priorities and approaches were largely in the hands of the U.S. organizations that provided the bulk of the financial resources.

A significant inaugural event highlighting opportunities for cooperation was a conference in Kirov in 1997. This conference brought together for the first time a number of important senior investigators from the United States and Russia who were responsible for research that involved highly dangerous pathogens (Box 2-1).

Then a significant pathfinder activity, which was to lead to larger investments

Box 2-1
International Conference in Kirov, Russia, on Severe Infectious Diseases

The Volga-Vyatka State Scientific Center of Applied Biotechnology, with the support of the International Science and Technology Center, brought together more than 50 specialists from more than 20 organizations in Russia and the United States, with Japanese scientists also participating, to discuss epidemiology, express-diagnostics, and prevention of infectious diseases. The group recommended accelerated development of vaccines, antiviral preparations, and antibiotics; greater use of molecular biology to design effective vaccines; and development of highly sensitive and specific methods of rapid diagnosis. The conference set the stage for continued international involvement in activities in Kirov and the neighboring territories, where former defense scientists could be brought together easily with other specialists in fields of mutual interest.

SOURCE: Proceedings of Conference, 1997. Complete reference cited in Appendix A.2.

that would support joint activities, was a series of eight pilot projects at two key Russian research centers during the late 1990s (Box 2-2). These projects demonstrated the feasibility of collaboration at previously closed Russian facilities while significantly redirecting capabilities of these facilities to civilian endeavors at a critical time of financial uncertainty. Following the success of seven of the eight pilot projects, the overall program was soon supported by the Russian government and several U.S. government agencies. As to the eighth project, further work on opisthorchiasis was not considered a priority by either side. Cooperation rapidly expanded and in time encompassed many different types of research at a number of research institutions.

Building on these early activities, the U.S. government devoted tens of millions of dollars annually, with Russian institutions contributing comparable levels of support, for biosecurity activities in Russia. Initially, the principal U.S. funder was the Department of Defense (DOD), which covered many of the direct costs of the programs. The direct costs that were covered by DOD eventually totaled more than $200 million. (See Appendix C.2 for the DTRA contributions.)

In addition, the Department of State (DOS) also began supporting biosecurity activities in Russia in the late 1990s. DOS gradually increased its contributions to a level of annual support of about $20 million during 2006. These funds were also focused primarily on covering a large segment of the direct costs. (See Appendix C.1.)

Box 2-2
Joint Pilot Projects Initiated in 1997

At State Research Center of Virology and Biotechnology Vector, Koltsovo

- Study of prevalence, genotype distribution, and molecular variability of isolates of hepatitis C virus.
- Study of monkeypox virus genome.
- Study of genetic and serological diversity of hantaviruses.
- Development of advanced diagnostic kit for opisthorchiasis.
- Study of antiviral activities of glycyrrhizic acid and derivatives against Marburg, Ebola, and human immunodeficiency viruses.

At State Research Center for Applied Microbiology, Obolensk

- Analysis of clinical strains of tuberculosis and mycobacteriosis.
- Investigation of immunological effectiveness of delivery in vivo of Brucella main outer membrane protein by the anthrax toxin components.
- Monitoring of anthrax.

SOURCE: *Scientists, Engineers, and Track-Two Diplomacy*, p. 51. Complete reference cited in Appendix A.2.

Other U.S. organizations launched smaller biology-oriented programs in cooperation with a variety of Russian research institutions and service providers, largely in the health and agricultural sectors.

U.S. government departments and agencies carried out most joint projects with interested Russian institutes through the good offices of the International Science and Technology Center (ISTC) in Moscow. Some research projects were financed through the regular contributions of the U.S. government to the core budget of the ISTC. The ISTC's partner program provided a second mechanism for international financing of projects that soon far exceeded activities supported by funds provided through the ISTC's core budget. (See Appendix E.2.)

Several dozen Russian production enterprises and research institutes that had been involved in the defense programs of the former Soviet Union were in difficult economic straits during the 1990s, as their budgets rapidly declined. Of particular importance was the fate of the Biopreparat complex, which had provided a research and production framework for the USSR's defense program. Box 2-3 describes Biopreparat's capabilities in the early 2000s, when the industrial conglomerate was beginning to recover following its near collapse during the 1990s.

Box 2-3
Biopreparat: An Early Focus of Redirection Activities

The joint stock company integrates 20 industrial enterprises that manufacture 1,000 different products. More than 36,000 workers are involved in production. Biopreparat accounts for 35 percent of Russia's total output of medical products valued annually at $280 million in drugs and $50 million in engineering articles. Biopreparat has four state research centers, six research institutes, two pilot design bureaus, and two design institutes. Its personnel number 6,000 scientists and specialists in microbiology, biotechnology, gene engineering, immunology, and biophysics.

SOURCE: Biopreparat Brochure, 2003.

By 2008, DOS had become the largest U.S. source of funding for biology-related nonproliferation projects in Russia, as DOD began to phase out its Cooperative Threat Reduction Program in the country. However, by this time the resources available to DOS were well below the earlier levels that had been provided by DOD or DOS.

For a number of years, within the budgets of DOS, some funds had been earmarked for use by the Department of Health and Human Services, the Agricultural Research Service, and the Environmental Protection Agency. Their common mission was to support activities in Russia that would redirect scientists who had worked on defense-oriented projects to civilian efforts in the technical areas of interest to the three U.S. organizations. The Russian government warmly welcomed cooperation with these organizations.

By 2012, annual expenditures by DOS for new cooperative projects related to biosecurity with Russian counterparts had declined to less than $1 million per year. Also, funds of the other three U.S. government agencies earmarked for support of bioengagement activities were no longer available. However, DOD was providing limited support to other government departments and agencies and universities to maintain a minimal level of contacts with scientific institutions in Russia.

Several other U.S. organizations have financed activities at lower levels to help prevent inappropriate proliferation of dangerous technologies developed in Russia. The largest contributor of these organizations has been the Department of Energy, which has supported a number of bioengagement projects that were designed to lead to commercial activities. The Global Initiatives for Proliferation Prevention has been the source of the funding (see Appendix C.3). In addition, a few projects with limited scope were financed by private foundations, such as the Nuclear Threat Initiative.

Gradually, Russian authorities were able to provide more funding for scientific cooperation within the framework of U.S.-supported nonproliferation programs. By 2008, many of the difficult biosecurity concerns had been addressed jointly, particularly upgrading physical security systems within selected Russian institutes. However, the issue of consolidation of pathogens within institutes and within clusters of institutes was a concern that, in the view of the U.S. government, did not receive the attention that it deserved.

Throughout the lifetimes of the foregoing nonproliferation programs, the focus of cooperative efforts increasingly emphasized the scientific benefits from cooperation. Special attention was given to strengthening approaches to commercialization of technologies and to promotion of transparency. Of course, the more traditional nonproliferation approaches, such as enhanced physical security, continued to be important to both governments and to Russian institutes that were slowly recovering from economic difficulties.

In general, over the years, Russian institutions developed and implemented several types of nonproliferation projects within the framework of programs supported by several U.S. government agencies. These programs were intended to

- Dismantle portions of Russian facilities that had the capability to produce large quantities of anthrax and other pathogens of concern. However, only one significant activity was carried out in Russia—at the Sibbiopharm facility in Berdsk. (See Box 2-4.) A primary focus for this type of activity in the region was U.S. support for dismantlement of other facilities in Kazakhstan.

Box 2-4
Conversion of Sibbiopharm Production Association Facility at Berdsk, 2006–2010

The Department of State contributed significant funding in helping to convert a facility of concern into a pharmaceutical production facility that produced enzymatic preparations used by the feedstuff, plant protection, and food industries. Several large fermenters capable of producing material of defense interest were dismantled, and the entire facility was modernized, including installation of new equipment, renovation of selected premises, and provision of technical consultations on commercial aspects.

SOURCE: Civilian Research and Development Foundation, which assisted the Department of State in implementation of this project, March 2012.

Box 2-5
Examples of Institutes Where Physical Security Upgrades Were Installed

- State Research Center of Virology and Biotechnology Vector, Koltsovo
- State Research Center for Applied Microbiology, Obolensk
- All-Russian Research Institute of Phytopathology, Bolshie Vyazemy
- Federal Center of Toxicological and Radiation Safety, Kazan
- Federal Center for Animal Health, Vladimir
- Plant of Biopreparations, Pokrov

SOURCE: Russian senior science manager, 2011.

- Increase physical security at Russian facilities where dangerous pathogens were stored and/or used for research and related purposes. Dozens of projects were implemented. (See Box 2-5 for examples of the Russian facilities that were involved.)
- Support research and related activities that would utilize the skills of the Russian workforce, and particularly the skills of former defense scientists, to strengthen the basic and applied research infrastructures of Russia. This support was substantial and extended into pilot production of medical and agricultural-related items. (See Appendixes C.1, C.2, C.3, and C.4 for examples of activities.)
- Carry out consultations and related activities concerning disease surveillance capabilities and outbreaks of infectious diseases of regional and global concern. Both countries had extensive surveillance capabilities in place. The cooperation was directed in large measure to rapid and reliable diagnostics, synchronization of surveillance approaches among different countries and with the World Health Organization (WHO), and standardization and distribution of surveillance data.

The focus of cooperative biosecurity programs involving a number of U.S. and Russian organizations gradually broadened. The two sides agreed that the best way to reduce the likelihood and consequences of misuse of dangerous pathogens—whether naturally occurring or illicitly obtained by malcontents—was to strengthen the overall public health system of Russia and the supporting scientific infrastructure. The emphasis was on development of approaches that would assist in the prevention, detection, diagnosis, and therapy of infectious diseases, whatever the sources of the diseases.

The joint activities that evolved covered a broad swath of projects. From the outset, cooperative research projects were high on the priority list. Initially, there was little cooperation to upgrade surveillance systems, but during the early 2000s, considerable emphasis was placed on coordination of capabilities to detect and respond to outbreaks of diseases at an early stage and to limit their subsequent spread should such outbreaks occur. In short, while the early emphasis was to develop projects that had direct relationships to proliferation and bioterrorism concerns, the scope of activities rapidly diffused to effect more traditional outcomes of human and animal health activities that are addressed in the next three chapters.

Appendix C.2 presents one set of DOD's indicators of progress in improving biosecurity at individual Russian facilities. The appendix also identifies a number of cooperative research projects carried out on the basis of their potential contribution to improving the research infrastructure of the country, where appropriate research activities could be implemented in a transparent manner.

An activity that commanded considerable attention for a number of years throughout the international security community was a collaborative program to investigate the properties of variola virus strains that have been preserved in both Russia and the United States. This effort was undertaken at the Russian research center Vector. It was directly related to ongoing discussions at the WHO as to whether all remaining smallpox isolates should be destroyed or whether it was important to continue to investigate the properties of the virus. Better understanding of smallpox diagnostics and medical countermeasures was considered important in the event that the contagious disease reappeared as the result of (a) accidental release of the organism into nature from Russian or U.S. WHO-approved stocks or (b) intentional release from other currently unknown and unapproved stocks (Box 2-6).

Many cooperative research activities carried out within the framework of nonproliferation programs were of considerable interest to the civilian research communities in a number of countries. For example, brucellosis is a disease of considerable concern in the agriculture field. Joint efforts within the framework of nonproliferation programs advanced scientific understanding of the characteristics of that particular disease (Box 2-7). Other common diseases were also addressed in the program, and some are highlighted in Chapter 3.

As collaborative programs developed and expanded, DOD and interested Russian institutions organized a number of international conferences and workshops that focused on bioproliferation concerns and the opportunities for cooperative research activities. The conferences, in particular, had a significant impact by helping transform previously isolated programs into reoriented transparent activities of worldwide interest.

In particular, during the early 2000s, DOD supported several international conferences directed to research at Russian institutions involved in U.S.-Russian collaboration. Hundreds of investigators from Russia, from other areas of the former Soviet Union, from the United States, and from Europe reported on cooperative projects (Box 2-8). The Russian project implementers were particularly

Box 2-6
Investigations of Variola Virus at Vector (2000 to 2006)

Research studies of the genomic structure of different variola virus strains were carried out. Also of interest was the identification of potential antiviral drugs that might hold promise for the treatment of smallpox. These studies were generally successful despite delays in the approval processes in the two countries to initiate and continue activities, problems involved in delivery of funds to the researchers, difficulties encountered in exchange of reagents, and interruptions of effective communications between the Centers for Disease Control and Prevention and Vector. Cooperation on specific research projects ended in 2007. Still, the projects provided important research data for the international community and had a significant impact by establishing lasting ties among researchers from the two countries.

SOURCE: Personal observations of committee members of activities from 2000 to 2006, 2011.

BOX 2-7
Collaboration in Research on Brucellosis

For several years, U.S. agencies supported research on vaccines that would counter the spread of brucellosis through cattle and other herds in Russia. Also of concern was the infection of bison herds in the United States. Progress was made in limiting the spread of the disease through improvement of the vaccination procedures in Russia. Comparative research studies identified the most promising Russian and American brucella vaccines for prophylaxis in cattle as well as in wild animals.

SOURCE: Former Scientific Adviser for DOD programs, February, 2012.

appreciative of these opportunities to stay abreast of important international developments of direct relevance to their research interests. For their part, the Russian investigators quickly improved the content and quality of their scientific presentations at the conferences as they became accustomed to participation in such international gatherings.

Box 2-8
St. Petersburg Conferences: International Outreach Opportunities for Russian Investigators

On four occasions, DOD assembled in St. Petersburg the principal investigators on research projects supported by DOD throughout Russia and other countries of the region. The Institute for Highly Pure Biopreparations hosted the conference sessions. These conferences were well attended, and opportunities for informal interchanges set the stage for follow-up consultations. In later years, the conferences were increasingly oriented to activities in other countries that had emerged from the Soviet Union. They were held outside Russia—in Germany and Atlanta, for example—and each involved only several Russian scientists. In brief, the networking benefits of the St. Petersburg conferences had a profound impact and are well remembered by both American and Russian attendees.

SOURCE: Observations by committee members who attended conferences, 2011.

In the early 2000s, DOS developed several programs that built on and expanded the early efforts of DOD. These DOS programs had the objective of commercialization of results of research to provide both long-term career opportunities for biological scientists interested in civilian applications and new income streams for important research groups. (See Appendix C.1.) Some specific activities are discussed in Chapter 4, which addresses applications of research results.

Throughout this period, the ISTC with support by U.S. government departments and agencies organized many training programs for Russian specialists engaged in cooperative projects. In this regard, the following topics were considered particularly important, beginning in the late 1990s:

- Good Laboratory Practices
- Good Manufacturing Practices
- Care and Use of Experimental Animals
- Institutional Review Boards for Research on Human Subjects
- Commercialization of Technologies

Now, with shrinking budgets of both the United States and Russia to engage bilaterally in nonproliferation activities, the outlook for future collaboration involving traditional approaches to biosecurity is not bright. At the same time, both the U.S. and Russian governments recognize that important aspects of biotechnology could be misused and that there is a clear imperative for international efforts to promote within the international life sciences community the concept of **transparent and responsible science.** The ISTC has adopted this theme as one of its most important activities prior to closing its doors in Moscow. It should not be difficult to obtain widespread international support for the concept.

While considerable progress has been made in reducing highly visible security problems, responsible research in the life sciences can only be adequately addressed on a global basis through long-term educational and practical programs, together with hands-on experience in the laboratory. The two countries with the most experience in handling especially dangerous pathogens and other biological materials are in a unique position to join forces in promoting life sciences in a highly visible manner at the bench and in production facilities, both at home and abroad.

Finally, most officials and scientists in both the United States and Russia who are familiar with bioengagement approaches to promote nonproliferation consider that the segregation of former defense scientists into a special class of participants in joint projects has long been outdated. *Capabilities and responsibilities* of investigators, not former employers of scientists, should comprise the key criterion that is used in selecting participants in cooperative activities.

The foregoing discussion leads to two important conclusions.

1. *The pioneering efforts of the two governments were important in helping to ensure that collaboration in research, testing, and use of potentially dangerous pathogens is carried out in a responsible manner, and they offer important lessons for the broader international scientific community. Responsible science requires transparency that accompanies international connectivity.*

Efforts to spread the culture of biosecurity and biosafety throughout the two countries and beyond can build on successful efforts demonstrated by many joint research projects of the past as well as by national efforts. At the same time, leading Russian and American scientists can play active roles in the international debates on handling the results of research on the influenza A/H5N1 virus and other viruses that could unexpectedly raise concerns over potential dangers to humans. Since the fall of 2011, there have been extensive international debates over the publication of results of studies of the influenza A/H5N1 virus, with American and Russian investigators playing important roles in the debates. (See Box 2-9.) Such debates will surely be pathfinders for handling other controversial findings as research on dangerous pathogens intensifies.

2. *Research to improve characterization, prophylaxis, and therapy of especially dangerous pathogens has had a significant and lasting impact on many related efforts.*

Periodic consultations among government specialists on especially dangerous pathogens are important. At times, new research activities may be warranted, such as is the case with the variola virus. When research is being considered, the

Box 2-9
Research Investigations of Influenza A/H5N1 Virus

The preponderance of the evidence from clinical, seroepidemiologic, and laboratory studies supports the notion that HPAI H5N1 viruses now circulating are extraordinarily lethal to humans compared to other influenza viruses.

SOURCE: Eric Toner and Amesh Adalja, "Is H5N1 Really Highly Lethal?" *Biosecurity and Bioterrorism*, Vol. 10, No. 2, 2012.

involvement of the international scientific community, and particularly the WHO, may be important. Given the broad experience of American and Russian scientists in addressing such issues, their participation can provide an important core of expertise for such international consultations.

FROM SECURITY TO SCIENCE AND TO APPLICATIONS

In the chapters that follow, other projects that were funded within the framework of nonproliferation programs are highlighted, even though the chapters are devoted to scientific advancement and to applications of research results in the public- and private-sector marketplaces. This is a welcome outcome of joint security-oriented efforts. Nonproliferation efforts are most significant when the approaches that have been adopted are continued. Contributions to science and to success in responding to market demand are good indicators of the likelihood of long-term support.

3

Advancing the Frontiers of Biological Research

Since the mid-1990s, thousands of Russian biological scientists and hundreds of American counterparts have been involved in cooperative research projects that have advanced the frontiers of biological research. Initially, the U.S. government covered almost all direct costs of cooperation. In recent years, Russian institutions have increasingly shared these direct costs, although in most areas their financial contributions still lag behind U.S. contributions. A few examples of significant cooperative research projects are presented in this chapter. Many other important research projects are chronicled in Appendixes C.2, C.3, and C.4.

One common indicator of mutual interests in cooperative research is the number of publications coauthored jointly by scientists from two or more countries. As set forth in Appendix F.1, American coauthors cited along with Russian coauthors have been very important for Russian scientists. Data for recent years shows that 11.5 percent of all coauthors who have collaborated with Russian coauthors have been from the United States. On the other hand, in general, Russian coauthors have not been very important for American scientists. Less than 0.4 percent of all coauthors who have collaborated with American coauthors have been from Russia.

At the same time, based on observations of research in Russian laboratories during the past decade by well-qualified American scientists, publications by Russian scientists—whether coauthored or authored independently—have not adequately reflected the achievements and potential of Russian researchers in the biological sciences. Clearly, Russian scientists need to give higher priority to publications in journals that meet international peer review standards, with particular attention to more detailed reporting of methodologies and accumulated data.

Committee members are familiar with details of a number of recent

U.S.-Russian cooperative projects. Thus, this report relies in large measure on their personal observations, supplemented with views of a number of research managers in the two countries, in reaching conclusions as to the importance and shortcomings of various approaches to cooperative research in the biological sciences. While the significance of different research activities varies greatly, joint efforts have contributed in a variety of ways to advancing science, to strengthening the scientific infrastructure of Russia during a critical economic period for the country, and to setting the stage for future collaborative efforts.

The majority of cooperative research activities have been carried out in Russia, with significant financing by U.S. organizations. However, U.S. support of Russian-based research projects that were justified in the first instance on the basis of countering proliferation has almost vanished. Current plans of the two governments indicate additional reductions of cooperative research, however justified, are in the offing. As a positive trend, on the other hand, more even balances in the funding and location of joint activities are receiving serious consideration.

In particular, U.S. funders are increasingly reluctant to cover Russian salaries and equipment to be used for research at Russian institutions, given the improved financial situation in Russia. At the same time, a small but steady influx to the United States of Russian researchers invited to be temporary researchers at National Institutes of Health (NIH) facilities, U.S. universities, and other research settings in the United States will undoubtedly continue. But the magnitude of these types of support from U.S. programs is not great. For example, in recent years, less than 2 percent of NIH grants that were awarded to foreign scientists were given to applicants from Russia.

The recent decline in U.S. financial support for collaborative efforts has been disappointing for some researchers from both countries, particularly for those who have benefited from past cooperation but are no longer successful in finding support for continuing their collaborations. While the researchers in the two countries may have interesting ideas for future cooperation, current and anticipated budget reductions mean that some potentially valuable programs will not go forward. But judging from past experience, the impact from even a reduced number of activities that are jointly designed, successfully pass through peer review, and are then implemented should be substantial.

MOTIVATIONS FOR COLLABORATIVE RESEARCH

In past years, officials in the two countries dealing on a daily basis with proliferation issues were interested in involving former Russian defense-oriented scientists in high-quality, civilian-oriented research activities for at least two reasons. First, permanent redirection of scientists from defense-oriented to civilian careers requires their establishment of personal scientific reputations within the civilian research community so that the redirected scientists will be able to compete successfully for funding from many sources over the long term. Second, a broad understanding of the characteristics of dangerous pathogens—which is the strong suit of a number of former defense scientists—is important in preparing to deal with disease outbreaks that are attributable to natural causes. Many cooperative projects that have been undertaken in Russia, pursuant to the U.S. focus on preventing proliferation, have also made significant contributions in advancing scientific understanding of interest to both countries.

An example of the close ties between research activities for nonproliferation and for scientific advancement is illustrated by investigations of bacteriocins at a former defense-oriented facility, the State Research Center for Applied Microbiology in Obolensk. The research was designed to engage former defense scientists in seeking an alternative to agricultural antibiotics. An important result has been development of a patentable product (see Box 3-1).

Also of importance have been institutional-support efforts financed in large measure by the U.S. government to strengthen capabilities of a number of research teams throughout Russia. Breeding of laboratory rodents in Russia, highlighted in Box 3-2, is an example of a project that has enhanced Russian institutional capabilities to conduct important lines of research.

At times, Russian research teams, working with collaborators from the United States and other countries, have achieved results of fundamental importance. They have created laboratories of research excellence of worldwide interest. Looking to the future, an example is the investigation of proteome (Box 3-3). Reflecting on the past, an example is the sequence of the variola minor for the first time (Box 3-4).

A number of Russian research teams that received continuing support from U.S. organizations over many years had strong backgrounds in investigating dangerous pathogens. (See, for example, Appendix D.1 concerning activities

Box 3-1
Research on Bacteriocins

Beginning in 2004, a team of American and Russian researchers developed bacteriocins, which are natural proteins produced by competing nonpathogenic bacteria that destroy *Campylobacter* in the intestines of farmed poultry, dramatically eliminating pathogens. Laboratory tests have shown that treated birds have *Campylobacter* populations that are millions or even billions of times lower than the populations of untreated birds. The research resulted in patent applications that could in time lead to alternatives to antibiotics in both the veterinary and medical fields.

SOURCE: Agricultural Research Service, January 2012.

Box 3-2
Accreditation of Laboratory Animal Breeding Facility, 2004

The Association for Assessment and Accreditation of Laboratory Animal Care International awarded full accreditation to the SFP Animal Care Breeding Facility at the Pushchino Branch of the Institute of Bioorganic Chemistry. Its initial activities were limited to rodents. Benefits of accreditation include international recognition of the quality of the activities; inclusion of the new capabilities in international directories and publications; and eventually use by Russian researchers of internationally accepted approaches for support of their activities.

SOURCE: *Biological Science in Russia*, p. 74, 2007, cited in Appendix A.2.

Box 3-3
Human Proteome Project (linked to the Human Proteome Organization plasma protein project)

This project is to characterize the proteins encoded by the human genome. The roadmap section that is to be established by Russian scientists is to identify the proteins encoded by genes of chromosome 18. There will be pilot and master phases. The pilot phase is to identify at least one protein for each gene and determine the level of its expression and predominant modifications. Data will be obtained on individual variability of the proteome in blood plasma and liver tissue. The master phase will include experimental revelations of the modifications for all proteins of chromosome 18. Russia plans to establish technologies for proteomic studies integrating mass-spectrometry with atomic microscopy. American partners are the University of Michigan and the Institute of Systems Biology (Seattle).

SOURCE: Russian research manager, September 2012.

and international interests of Vector, and Appendix D.2 concerning activities of the All-Russian Institute of Phytopathology). In other settings, Russian teams have long-term histories of civilian-oriented activities, although they have been sensitive to the possible diversion of technologies to inappropriate uses (see, for example, Appendix D.3 concerning the Research Institute of Influenza).

Box 3-4
Sequence of the Variola Minor Virus Genome DNA

During the late 1990s and into the early 2000s, scientists from Vector and the Centers for Disease Control and Prevention collaborated in the determination of the genomic sequences of a number of smallpox viruses. The work was carried out at the early stages of the genomics revolution when the genomic signature of most pathogens remained unknown. This historic accomplishment led to an international debate on the need for retention of live variola virus at the two centers designated by the World Health Organization as repositories for the remaining strains of smallpox viruses.

SOURCE: Department of Molecular Biology of Genomes, Vector, 2000.

ORGANIZATIONAL AND FINANCIAL INTERESTS IN BIOLOGICAL RESEARCH

From the Russian perspective, the political and financial situations in 2012 are dramatically different from the situations 10 to 15 years earlier. Now, the Russian government is reluctant to carry out projects that are of major interest only to the United States, which was commonplace throughout the Russian scientific community when funds were scarce. The concept of true partnerships is evolving, which is a healthy development.

Characteristics of such partnerships are set forth in Box 3-5. New programs to this end have been established by the Russian Ministry of Education and Science, acting through Russian research universities, and by the Russian Foundation for Basic Research, which finances small research projects throughout the country. U.S. government agencies (e.g., the National Science Foundation [NSF] and NIH) also provide opportunities for bilateral cooperation. However, except for support of joint programs in AIDS-related research sponsored by NIH, the U.S. government has not put in place cooperative programs that have been established specifically to support U.S.-Russian cooperation in the biological sciences and at the same time are broadly available to interested applicants through a competitive process.

A number of bilateral governmental agreements and memoranda of understanding are in place to provide frameworks for cooperation in biological research. (See Appendix B) The broadest agreement is the long-standing U.S.-Russia Science and Technology Cooperation Agreement, which provides an umbrella for research activities of interest to a number of government agencies in the two countries that have like-minded partners in the other country. An example of a

Box 3-5
Characteristics of Effective Partnerships

- Common interests and common goals.
- Joint planning and joint decisions concerning project design and modification as necessary.
- Equitable sharing of costs and fiscal responsibility.
- Frequent interactions—electronically and in person.
- Equitable sharing of results of collaboration, including joint authorships and sharing of rights to intellectual property that is developed.

SOURCE: NRC Report on the Biological Threat Reduction Program, p. 69, 2007, cited in Appendix A.2.

Box 3-6
Long-term Census of Arctic Waters, Air, and Life-forms

In the summer of 2009, the Russian oceanographic vessel *Professor Khromov* transported 50 scientists, primarily from the United States and Russia, into reaches of the Bering Sea that are particularly sensitive to climate change. For 6 weeks, they collected samples of air, water, and life-forms, which involved dragging heavy nets along the sea floor to obtain bottom-dwelling organisms. They also observed fish and crabs that survived the unfavorable northern conditions as they measured currents, temperatures, and salt content. Such periodic joint investigations are an important aspect of global efforts to understand climate change that affects the fishery, environmental, and other interests of countries of the northwest Pacific region.

SOURCE: National Oceanic and Atmospheric Administration, 2011.

program carried out under this agreement calls for biology-oriented investigations of the Bering Sea. (See Box 3-6.)

As to memoranda of understanding or other types of government-to-government agreements, many departments and ministries have such arrangements with their counterparts. An unusual arrangement is the agreement between NIH and the Russian Academy of Sciences, which presumably will actively involve both government and nongovernment organizations. (See Box 3-7.)

Box 3-7
U.S.-Russia Scientific Forum

- Umbrella agreement between the U.S. Department of Health and Human Services and the Russian Ministry of Health and Social Development.
- Agreement between the National Institutes of Health and the Russian Academy of Sciences (plus other partners from both countries).
- Annual meetings and smaller workshops on selected biomedical topics.
- Topics of initial interest include cancer, cardiovascular diseases, infectious and rare diseases, and translational research training.

SOURCE: NIH, June 2012. (See Appendix F.5.)

INDIVIDUAL INVESTIGATORS

While centrally managed exchanges receive much of the publicity about cooperative activities, an important backbone of bilateral research cooperation has long been the activities of individual scientists who seek out and maintain contacts with colleagues with similar interests. They obtain financial support from whatever sources are available at critical times in their activities. Sometimes they simply resort to e-mail correspondence, to side meetings at international conferences, or to privately organized visits to the laboratories of their colleagues. Ideally, they have in place a mechanism that will help ensure continuation over a number of years.

A particularly successful program in fostering such direct contacts of young investigators in the biological sciences was a program organized by the Howard Hughes Medical Institute in the late 1990s and into the early 2000s. It has been credited with being the springboard for successful careers of a number of promising young biologists at Russian institutions. (See Box 3-8.)

Grants by NIH, and occasionally by NSF, to support individual U.S. and Russian scientists working together are sometimes important. (See Appendixes C.5 and C.7.) American scientists are sometimes eager to add a Russian dimension to their projects, particularly if this outreach provides access to unique Russian expertise. And in recent years, the Russian Ministry of Education and Science has been providing Russian universities with funds to reach out and engage leading western scientists in their activities. Also, both sides have facilitated participation by scientists from the two countries in selected international meetings.

Now an increasing number of Russian senior scientists are becoming regular hosts for international visitors. For example, Appendix D.4 identifies many out-

Box 3-8
Support for Early-Career Russian scientists (1995–2005)

In 1995, 2000, and 2005, the Howard Hughes Medical Institute awarded a total of 25 grants to Russian investigators, along with grants to investigators from other countries, to explore cutting-edge topics in biology-related fields. The awards provided up to $500,000 for 5 years, to be used to support relatively young principal investigators and, to the extent appropriate, their research teams. The principal investigators could travel abroad, but only for short periods of time. In the biology-oriented city of Pushchino, for example, the awards kept important laboratories functioning at a time when the institutes were on the verge of collapse. They in effect saved important research programs in the poverty-stricken town.

SOURCE: Observations in Russia by NRC staff, April 1999.

Box 3-9
Pathogens That Destroy Important Crops

U.S. agricultural scientists, working in cooperation with Russian colleagues, for the first time developed a general map of plant diseases in Russia, including molecular characterization of the most diverse among 2,000 collected strains. They uncovered new strains of pathogens dangerous for potatoes, cereals, sunflowers, and mustard crops.

SOURCE: Vavilov Institute of Plant Industry, September 2011.

reach activities of institutes of the Siberian Branch of the Russian Academy of Sciences. Some interlocutors spend considerable time interacting with scientists both in their laboratories in Russia and in collaborating laboratories in the United States. Still, these limited activities that are focused on U.S. institutions pale in comparison with (a) much greater travel between the United States and the countries of Europe and (b) exchanges involving Russian and European scientists who take advantage of easy travel connections.

Another aspect to be taken into account in addressing collaborative research activities is the common practice of dividing scientific research into basic and applied categories. Box 3-9 presents an example of research that straddles the border.

THE WAY AHEAD

Many forms of collaboration have paid off in the past and offer opportunities for the future. Usually, collaboration has been most productive when the participants have frequent opportunities to spend time together. E-mail, Skype, international meetings, brief visits to counterpart laboratories, participation in expeditions, and many other channels for contact come into play. Only the researchers know when collaboration is paying off. Their views on moving forward are critical, and they should have a loud voice in planning future activities.

There is little likelihood that the level of bilateral cooperation in basic research that was reached during the past decade will soon again be attained. Neither country currently has large budgets for international research activities. But with each demonstration of successful engagement, the case for thinking globally and focusing on those opportunities wherein the potential returns on investments are highest should lead to increased support for U.S.-Russian collaboration.

The following conclusion recognizes the many common interests and complementary strengths in basic science in the two countries and the importance of the two countries being effectively engaged in scientific areas of increasing interest. Scientists from both countries have good track records in opening new trails for investigating topical areas as they emerge on the scene. The objective of cooperation in biotechnology as a route to commercial success with economic payoffs for both sides depends to a considerable degree on basic research capabilities of the two countries. Finally, cooperation in basic research can provide access by U.S. scientists to novel ideas of strong counterparts while upgrading Russia's capabilities to innovate that currently lag behind the capabilities of a number of other countries.

A number of governmental and nongovernmental research centers in both countries will be increasingly interested in the returns on investments in collaborative basic research that draws on the strengths of the two countries in fields of increasing international interest, such as the areas of common interests set forth in Chapter 10.

4

Applications of Science in the Public and Private Sectors

Joint efforts in basic research have usually been linked, at least conceptually, to long-term aspirations for achieving tangible benefits tomorrow from investments today in science. This chapter considers bioengagement programs designed to facilitate the applications of science in supporting economic and social activities of the two countries, as well as addressing security concerns, in both the near term and the long term. The emphasis is on (a) upgrading science-based services provided by governments and (b) introducing new commercial products developed by Russian institutions as the country tries to more fully embrace a market economy. Both aspects are important to the United States, as well as to Russia, because U.S. organizations are searching for opportunities to play a constructive role in the outreach activities of Russian research and service institutions.

However, in all countries there are many failed attempts for the relatively few successes in introducing into public- and private-sector markets products and services based on development of advanced technology, and particularly biomedical products. With this experience, many U.S. firms have been reluctant to risk investments in an uncertain Russian business environment. At the same time, Russian entrepreneurs have limited experience in determining whether their proposed products and services are better or cheaper than competitive products, both at home and internationally.

In short, Russian entrepreneurs have difficulties convincing potential U.S. partners that eventual payoffs from collaborative activities are worth the financial risks. Unfortunately, Russian business organizations seldom are prepared to take the necessary time, which may extend over several years, to nurture a solid relationship with potential partners from abroad in order to develop and carry out plans that will improve the likelihood of business success. Nevertheless, there are increasing signs of progress for bioengagement in the private sector, as well as when funding for public-sector activities is available.

OVERARCHING EMPHASIS ON GOVERNMENTAL SUPPORT FOR APPLICATIONS OF SCIENCE

Joint ventures and other types of private-sector investments have been limited in size and scope. A number of private-sector bioengagement activities have been oriented to achieving near-term payoffs that would benefit segments of the populations of the two countries in discernible ways. This has been an admirable but elusive objective.

The marketing of products of research developed at biology-oriented public-sector research institutions began slowly in Russia during the late 1990s. There were few technologies that Russian researchers could offer at competitive prices or with significant quality improvements over imported products and services. Unfortunately, the rhetoric by western optimists as to growing opportunities for commercializing Russian technologies for the new economy raced ahead of market realities. "Made-in-Russia" was a label that seldom attracted large numbers of potential buyers.

Thus, until now, government-supported programs in Russia have usually been an important aspect in the realization of near-term applications of the results of bioengagement. At times, public research institutes have operated like small businesses in selling their products. For example, a research institute in Vladimir has a substantial animal vaccine business that competes with private companies. The institute's company serves as a conduit to the marketplace for promising research results.

Overall, much of the bilateral cooperation on applications of science has focused on three types of activities in Russia: (1) improving services of broad interest to the population that are provided through governmental institutions and scientific centers—in the fields of health, agriculture, and environmental protection; (2) strengthening capabilities of Russian institutions to begin to commercialize their technical achievements that would be of interest in the emerging private markets within Russia, and later in the global marketplace; and (3) supporting new components in the research and development (R&D) chain that are important for the commercialization of biomedical, agricultural, and other technologies.

New institutional components include the mega-incubator to be located at Skolkovo near Moscow, together with supporting incubators in other cities throughout the country and abroad; the state-owned enterprise Rusnano, which has development of biomedical technologies on its list of priorities; and various venture capital funds in Russia, which are also targeting the biomedical sector. These new entities are intended to attract widespread interest concerning the benefits to both the public and the private sectors in Russia of engaging advanced-technology Russian scientists along with specialists from the United States and other countries. (See Appendix F.3 for an overview of Russia's ambitious plans for developing the pharmaceutical-biotechnology sector.)

All the while, U.S. pharmaceutical and biotechnology companies continue searching at home and abroad—with considerable success—for new opportunities to apply scientific findings to development of marketable products. A few international companies have recognized the strong research capabilities of individual Russian scientists as well as teams of scientists, and they are interested in engaging with selected groups of Russian researchers. However, most U.S. pharmaceutical and biotechnology companies consider investments in other countries to have higher prospects for economic returns during the next decade. Thus, they are concentrating most of their efforts elsewhere.

In a few cases, U.S. companies have enlisted Russian partners that have contributed their technical skills in developing the technological basis for market success. Still, applications of biotechnology in the private sector have been in large measure a one-way street. Technology has flowed to Russia from abroad as it tries to stay abreast of international developments. The tangible benefits to the United States have been sparse, limited to the incomes that U.S. companies can earn from selling their products in Russia. Nevertheless, the evolution of the Russian market attracts continued interest of the U.S. private sector.

A WIDE RANGE OF PROJECTS

This chapter highlights examples of approaches that Russian and U.S. partners have pursued to develop technologies that would be of interest to potential users, primarily in Russia. At the same time, Russian, U.S., and other international companies have been producing and selling a few items based on biological science and biotechnology innovations within Russia. Of course, many international firms have been vying for sales to the Russian government and regional governments of imported goods and services, while local companies and local entrepreneurs have difficulties winning open and fair competitions at the national, regional, and municipal levels. As emphasized above, they simply cannot offer competitive goods and services.

As noted in Chapter 2, more than a decade ago the U.S. government began exploring opportunities to engage Russian partners in conversion of biological production facilities from defense to civilian activities. The only significant effort in this area was the redirection of activities at the previously discussed Sibbiopharm facility in Berdsk. On a more modest scale, while upgrading physical security systems at the State Research Center of Virology and Biotechnology Vector, the U.S. government provided limited technical assistance for strengthening the production capability of the associated company Vector-BiAlgam in Koltsovo.

The Engelhardt Institute of Molecular Biology in Moscow took a different approach as it expanded its research activities into the public- and private-sector marketplaces. The institute made arrangements with Argonne National Laboratory, and eventually with Motorola and Hewlett-Packard companies, to develop and manufacture biochips that can detect the presence of harmful pathogens—particularly pathogens affecting patients in hospitals. Such biochips have been of interest to international companies for several decades, but the institute was able to add technological innovations to ongoing efforts at the Argonne laboratory that became commercially interesting. Biochips produced by the institute are now used in Russian hospitals to help identify the causes of various illnesses. (See Box 4-1.) However, large multinational firms continue to dominate markets throughout the world.

Taking yet another approach, in the early 2000s, the Department of State (DOS) decided to support several Russian institutions that seemed to have potential for manufacturing products that would be accepted in Russian markets and in markets of neighboring countries. Continuation of research and development activities initially financed by the United States at the institutions was the objective. The program began with a number of educational seminars and training programs. DOS then expanded on these activities as it launched the BioIndustry Initiative discussed in Appendix C.1. Box 4-2 sets forth an important comment by a director of a major Russian institute on the significance of this initiative. This activity helped his institute obtain recognition for Good Laboratory Practices and Good Manufacturing Practices, as a prelude for profitable production of several lines of drugs.

Turning to outreach activities of well-established Russian research institutes, the Central Research Institute of Epidemiology in Moscow has developed kits for detecting and characterizing the presence of a variety of diseases, at times with support from U.S. partners (Box 4-3). There are other commercialization successes flowing from joint U.S.-Russian efforts. In some cases, the Russian Foundation for the Support of Small Innovative Firms (the Bortnik Fund) has helped facilitate entry into important markets for joint undertakings.

But overall, the number of profitable commercial ventures with long-term

Box 4-1
Biochips for Identifying Causative Agents of Serious Diseases

With funding from four U.S. and three Russian organizations, the Engelhardt Institute of Molecular Biology developed an assay that takes 18 hours in contrast to the standard 6–10 weeks. The technology can be used to assess causative agents of TB and MDR-TB, HIV, hepatitis B and C, influenza, and other important diseases.

SOURCE: Engelhardt Institute of Molecular Biology, 2011.

Box 4-2
Building on Cooperative Projects

"We are just as interested in maintaining contacts with American specialists as in financial support from the United States. Interactions of specialists are very important in staying abreast of developments in the field and in continuing research efforts initiated through the U.S. Government as we begin to sell our products on the commercial market."

SOURCE: Director of former Biopreparat Institute, 2006.

Box 4-3
Marketing of Diagnostic Kits

The Central Research Institute of Epidemiology, with assistance from American partners through the International Science and Technology Center, established a small enterprise, InterLabService, which now produces kits for testing for the presence of a variety of disease pathogens. Relying on traditional scientific outreaches of the institute throughout Russia and neighboring countries, the enterprise has developed a profitable and growing market for its products, which successfully compete with kits offered by other organizations in Russia and abroad.

SOURCE: Senior manager of the Center for Molecular Diagnostics, 2011. Also, www.epidemiolog.ru/ and www.interlabservice.ru/en/about/index.php.

lifetimes that have emerged from research institutions in Russia has not been great. Financing is difficult. Management skills are in short supply. Security requirements are sometimes severe. Even Russian entrepreneurs who have received recognition for success in commercialization of their discoveries are recording only narrow profit margins.

In 2008, DOS launched a limited pilot program to help jump-start small biotech enterprises in Russia. For years, the lack of a vibrant small and medium business sector has been one of the reasons that Russia has not moved in a discernible manner toward its goal of joining the ranks of countries that boast knowledge-based economies. The purpose of the new program was to provide loan financing that would enable small Russian companies to take the early steps needed to move into the marketplace.

The approach called for a supportive Russian bank to make loans to prospective Russian biotechnology businesses, with DOS guaranteeing repayment of the loans. This approach had been successfully used by the U.S. Small Business Administration in supporting start-up companies in Russia in other fields, such as transportation services and food services, many years earlier.

A particularly successful recipient of financial support from the pilot program was the Russian biotech firm Biocad (Box 4-4). Other projects also succeeded in bringing new products into the commercial sector. Unfortunately, however, some projects encountered administrative difficulties, and the program was terminated, at least temporarily. Even though Russia is not accustomed to supporting risky propositions, the approach may deserve reconsideration as a novel way to move products forward. There will be failures. But if products are marketable and prices outweigh costs, there should be some successes.

In the agricultural field, Russian institutes and enterprises have had considerable success in providing the government and farming organizations with needed vaccines, antibiotics, diagnostics, and other animal medicines. A few firms have developed advanced technologies that have found their way into the marketplace. A good example of such a firm is NARVAC, which has long supported the agricultural community of Russia, at times in cooperation with U.S. partners (Box 4-5).

In another initiative, beginning in the mid-1990s, the U.S. Department of Energy (DOE) focused on redirection of Russian defense scientists to new

Box 4-4
Loan Financing of a Small Firm

Biocad is a small Russian biotech firm established in 2001. It has both R&D capabilities and full-scale manufacturing capabilities. In 2008, it received a loan of $2 million from a Russian bank to expand its manufacturing activities, with repayment guaranteed by the Department of State. The loan was repaid. In 2010, it had eight drugs on the market in the fields of gynecology, urology, and neurology. Now Biocad is a growing biotech company, selling patented medicines, biological analogs, and generics. In 2011, Biocad allocated $10 million to monoclonal antibodies, with plans to double its investments in 2012. Also in 2012, cooperation began with Pfizer to produce a drug to treat A-type hemophilia in Russia.

SOURCE: ISTC, May 2012. Also see Appendix C.1.

Box 4-5
Serving the Agricultural Community

NARVAC, an important Russian supplier of veterinary products, has for many years cooperated with researchers associated with the U.S. Department of Agriculture's Agricultural Research Service. It has developed a strong research and development capability to support its manufacturing activities, which now produce swine and other vaccines, as well as therapeutics and diagnostics for other animal diseases. As one example of the payoff from collaboration, NARVAC, working with American scientists, isolated Marek's disease virus from chicken flocks. These isolates were classified by pathotype (virulence) based on animal inoculation studies carried out in U.S.-designed Horsfall-Bauer isolation units constructed in Moscow. The chickens were from a pathogen-free flock maintained in Russia. The study provided the basis for an improved pathotyping assay that can be performed easily by many laboratories around the world. A key to this success was a series of reciprocal visits between the collaborating laboratories.

SOURCE: American researcher involved in project, 2011.

careers. The concept has emphasized the twinning of Russian companies and institutes with U.S. small companies that have comparable interests in specific products. The program, initially titled the "Initiative for Proliferation Prevention," spawned the United States Industry Coalition (USIC). USIC is a group of small American companies that have been interested in finding partners in Russia and other countries of the former Soviet Union to develop and produce commercially viable products but do not have the connections to initiate programs. With DOE laboratories serving as brokers of initial contacts between interested Russian organizations and members of USIC, partnerships for bringing to market viable technology-based products have been formed with varying degrees of commercial success. Over the lifetime of the program there have been about 150 projects carried out in Russia, with about 30 percent linked to the biomedical sector (Box 4-6).

Also, in April 2012, the ISTC reported other successful projects in moving biotechnology achievements of Russian institutions toward the marketplace. Two are noted in Boxes 4-7 and 4-8.

Finally, several foundations and nonprofit organizations headquartered in the United States have supported agriculture and health programs in Russia. While funding levels have been modest—usually less than $2 million annually, the

Box 4-6
Successful Commercialization Projects

About 20 percent of the projects financed by DOE can be considered as commercial successes, with a typical project costing about $700,000 over 2 years, including costs incurred by DOE laboratories that assisted in facilitating contacts. The interested U.S. company contributes one-half of the cost in cash or in-kind services. There have been marketable products in areas such as use of radioisotopes for medical treatment, rapid diagnostics techniques, drugs, crop protection agents, biodecontamination devices, and wound-healing treatments.

SOURCE: U.S. Industry Coalition, February 2012.

Box 4-7
Molecular Diagnostics for Mixed Tick-borne Infections

The Institute of Biological Instrument-Making, Moscow, working with the Centers for Disease Control and Prevention, developed a diagnostic system for detecting antigens of zoonotic infections in the blood of patients and in biomaterial from ixodid ticks, including their main hosts. Simultaneous detection of specific antibodies to agents of several tick-borne infections based on phosphorescence analyses was developed and validated. The approach enabled screening, seroepidemic, and diagnostic studies.

SOURCE: ISTC *Annual Report 2011*, p. 16, 2012.

results have had an important impact in encouraging greater bilateral or national efforts in neglected areas. See Boxes 4-9 and 4-10 for examples of (a) a privately financed initiative and (b) a private initiative that attracted support from the U.S. Agency for International Development. They have played constructive roles in upgrading Russian approaches for providing important services in the medical field.

Box 4-8
Preclinical Safety, Efficacy Testing, and Technology Transfer of Novel Compounds for Drugs

The following organizations have been working together: Center for Development of New Drugs (Orchemed), Institute of Physiologically Active Compounds (Chernogolovka), Medivation (San Francisco), University of California at Santa Cruz, and Tufts University. They have formed one of the few preclinical testing organizations with modern facilities in Russia. They have spawned a consortium of 13 Russian universities and their U.S. partners. They are now promoting promising technologies and support of the Russian pharmaceutical industry. This joint effort has supported presentation of Russian pharmaceutical products in compliance with international quality standards, thereby facilitating their routes to international markets.

SOURCE: ISTC *Annual Report 2011*, p. 15, 2012.

Box 4-9
Haemophilus Influenza Research and Vaccination Program

In 2010, the Vishnevskaya-Rostropovich Foundation completed studies that showed a significant burden of Hib meningitis in children, in both western Russia and the Far East. The foundation supported vaccination programs in Yaroslavl, the Murmansk regions, and Vladivostok. Over 70,000 children were vaccinated. As a result, the Hib vaccine has been added to the national vaccination calendar, and its administration is now financed by the Ministry of Health and Social Services.

SOURCE: Vishnevskaya-Rostropovich Foundation, March 2012.

TIME FOR BALANCING THE LEDGER

Most examples that are cited above and noted in the appendixes of this report focus on activities in Russia, with the U.S. side usually providing most of the financial resources for covering the direct costs of implementing joint projects. This approach can be traced back to the economic crisis of the 1990s and the pat-

Box 4-10
Cooperation in Continuing Medical Education

With funding from public and private sources, the American College of Physicians, in cooperation with medical education institutions in 13 regions of Russia, has sent 50 highly qualified American physicians to Russia during a 15-year period, where they have interacted with almost 10,000 Russian physicians. This service has increased the capabilities of the Russian physician community to manage serious diseases and reduce premature mortality. The program has also supported travel by 13 groups of Russian physicians to the United States for exchanges of experience.

SOURCE: American College of Physicians, 2011.

terns that emerged during the economic downturn in Russia. Now the economic situation is different. The character of the bilateral relationship needs adjustment to cost-sharing arrangements if the concept of joint partnerships for mutual benefit is to become widespread.

Both countries are interested in attracting foreign investors in development of products that can help support economic growth while providing cheaper and better products for sale locally and throughout the world. However, the levels of Russian investments in the biological sciences in the United States and of U.S. investments in Russia are quite small, although they are important in setting the stage for more ambitious efforts. They have often demonstrated a level of mutual interest in developing stronger commercial ties.

The governments are working together to encourage foreign investment in both directions by improving the legal and economic frameworks for foreign companies to conduct business in the respective countries. At long last, the issue of membership for Russia in the World Trade Organization has been resolved, and the commercial playing field has to a large degree been leveled. Intensification of engagement activities of companies from both countries is becoming more realistic. An interesting example of commercial engagement is set forth in Box 4-11.

Looking forward, the private sector needs to be a key player in spurring the transition of Russia toward a knowledge-based economy while enabling the United States and other countries to engage more effectively with the latent high-technology expertise in Russia. The Russian government is counting on state-owned firms to play an important role in this transition. As a starting point, several hundred state-owned firms are to provide 5 percent of their sales to support R&D activities in Russia. However, Russian skeptics question whether these

Box 4-11
Rusnano to Bring New Drug Manufacturing to Russia

Rusnano plans to team with U.S. investor Domain Associates in coinvesting in about 20 U.S.-based health care technology companies. Rusnano will invest up to $330 million, while Domain's venture capital funds and other investors will invest a comparable amount. Additional funds will be used to establish a pharmaceutical and medical device manufacturing facility in Russia, where products created by the recipients of Rusnano's investments will be manufactured.

SOURCE: *Reuters,* March 6, 2012, and Appendix E.5.

funds will be used effectively in enhancing the nation's research capabilities in the near term.

Finally, as previously discussed, the Skolkovo Foundation has engaged the Massachusetts Institute of Technology to contribute to the design and establishment of a new high-technology university that is to become one of the anchors at Skolkovo, near Moscow. At Skolkovo, Russia hopes to replicate important aspects of Silicon Valley. Strong universities have been important components of successful technoparks in Russia and in many other countries, although the planned scale of activities at Skolkovo far exceeds similar efforts in other parts of Russia. Biomedical research is one of five key areas of interest. (See Appendix E.4.)

Summarizing, the two governments can provide incentives for individual scientists, research teams, and commercial organizations to explore and propose new topics for bilateral cooperation. In principle, cooperation can be a driver of innovation that results in profit, particularly in Russia, where efforts to penetrate international markets have almost always encountered difficulties. Small- and medium-sized companies, in particular, need special encouragement to use their entrepreneurial skills in bringing new products to market. Thus, cooperation will require strong government involvement for years into the future.

SIGNIFICANT INITIATIVES

The value of applied science to government agencies in both countries and to the general public should not be underestimated. Every day, policy makers, regulators, and researchers rely on up-to-date scientific information that affects their responsibilities. Every day the general population awaits the miracle drug, the strength-enhancing nutrient, and the harmless-to-humans repellent of undesirable insects. Thus, cooperation should serve both the public and the private sectors, although this chapter has repeatedly highlighted the most difficult portion of the road—commercialization by the private sector.

Against this background of both public- and private-sector interest in applications of science, the committee reached two different but equally important conclusions.

1. Private-sector companies in each country, including state-owned Russian companies, will continue to need considerable government incentives to give greater attention to investment opportunities in the other country.

Over the years, there have been important examples of investments by U.S. firms in Russia and Russian organizations in the United States in areas other than biotechnology that have paid off for the investors. Lessons learned from these successes should be considered by the governments as they seek to promote international investments in both directions in biotechnology.

Several U.S. programs to link Russian research institutions with small U.S. biotechnology firms have been important, and particularly programs supported by DOE. However, protection of intellectual property being developed in Russia and intellectual property being considered for use by U.S. firms in their operations involving Russian organizations will be even more essential with the advancement of technologies. Also, the governments can work together to strengthen the legal framework for a business-friendly environment in Russia. Such steps are essential if expanded efforts of the private sector are to result in an increase in profitable undertakings.

2. *Cooperative environmental projects are now conspicuously absent from the list of bilateral activities. There are many opportunities to combine efforts in this field. Among the newly emerging tools for conducting assessments of environmental problems are computational toxicology and methodologies for environmental sampling over large wetland areas.*

Maintaining a stable environment can be a theme that unites scientific efforts of the two countries. While a focus may be on the biological sciences, the involvement of specialists from a wide variety of disciplines has become essential in carrying out many types of environmental assessments. The two examples cited above would attract scientists from a variety of specialties. And the long-term results of such activities could enhance the lives of significant segments of the populations in the two countries.

5

Programs with Regional and Global Reaches

In this report, the topics of nonproliferation (Chapter 2), advancement of science (Chapter 3), and applications of science in the private and public sectors (Chapter 4) have encompassed a number of bilateral projects with impacts beyond the borders of the United States and Russia. Set forth below are a few additional examples of bilateral efforts with particularly pronounced regional or global reaches. The activities that are described have been generally successful in terms of achieving scientific objectives, thereby eliciting significant regional and, at times, global attention. While some programs are likely to continue for the next several years, the longer-term financial outlook for bilateral cooperation that contributes directly to international science is uncertain.

As underscored in the Introduction of this report, both governments have made substantial financial contributions to joint efforts. These activities have often intersected with programs of international organizations, such as the World Health Organization, the Food and Agriculture Organization, and the United Nations Educational, Scientific, and Cultural Organization. At times, bilateral efforts have added momentum to more broadly based international programs with similar goals (e.g., HIV/AIDS programs). Also, bilateral initiatives can be important in jump-starting programs that had been developed within international or regional organizations (e.g., interest of the Arctic Council in black carbon effects on global warming). At other times, international organizations may be well positioned to encourage continuation of efforts rooted in joint U.S.-Russian initiatives.

While individual projects that are cited have been implemented bilaterally, the coordination of these bilateral projects with multilateral activities that address global or regional issues with closely related objectives has generally been quite good. Indeed, frequently the same national officials have responsibilities for both bilateral and multilateral activities with similar objectives. Also, at times, the U.S. and Russian governments have decided to highlight their bilateral activities at international meetings. Then they usually take steps to ensure that other interested parties are aware of their activities before they publicly announce success stories.

Set forth below are seven examples of bilateral activities with regional or global impacts.

1. *Leading the world in space biology*. The global leadership of the U.S. and Soviet-Russian manned-space programs is unquestionable. The two countries have been pioneers in developing space biology for the past 50 years. Lessons learned from U.S.-Russian efforts are gradually spreading to other countries interested in exploration of space.

During the past decade, considerable attention has been focused on a future manned mission to Mars. At the same time, the immediate challenges of operating the international space station have required the constant attention of Russian and American doctors, researchers, and other medical professionals. Several joint activities being planned for the near future are set forth in Box 5-1.

2. *Addressing HIV/AIDS*. Formal U.S.-Russian cooperation in addressing HIV/AIDS began in 1989 with a bilateral agreement between the U.S. Institute of Medicine and the Russian Academy of Medical Sciences. Shortly thereafter, the program was taken over by the National Institutes of Health and the Soviet

Box 5-1
Planned Joint Space Research Programs

- Isolation and confinement studies as analogs for long-duration crewed missions. Research topics include crew behavior, group interactions, crew performance, microbiological and immunological investigations, and clinical-psychological studies.
- Space radiation health studies, including risks of cancer, chronic tissue effects, acute radiation sickness, and changes in central nervous system functions.
- Analyses of robotic precursor missions to address toxicity issues that could affect human health.
- Russian free-flyer mission to address partial gravity and long-duration effects of microgravity on living systems.

SOURCE: NASA Headquarters, 2011.

Box 5-2
Reducing HIV/AIDS Problems in Russia

For more than 15 years, USAID provided financing and expertise for selected aspects of the large Russian-led effort to help control the level of HIV-infected patients. During the 1990s, the emphasis was on raising awareness of the problem, particularly among the Russian youth, and on training medical professionals to provide advisory services to vulnerable populations. More recently, emphasis continued to be on counseling services targeted on the most vulnerable populations, with special attention to infected prisoners and injection drug users.

SOURCE: USAID Moscow, February 2012.

Ministry of Health (now the Russian Ministry of Health and Social Services). The two governments have worked together in this field ever since.

In the 1990s, the U.S. Agency for International Development (USAID) initiated an important component of the overall HIV/AIDS effort focused on raising public awareness of the problems and advocating measures for combating the disease. (See Box 5-2.) This activity is now a component of the global effort of USAID to address HIV/AIDS issues in selected countries worldwide.

The investment by USAID in this effort has been several million dollars per year for more than a decade. However, this level of investment has been small in comparison with the Russian investments in the overall effort. Also, international programs such as UNAIDS and programs of other governments have long supported significant efforts in Russia, and coordination with activities of others has been an essential dimension of the joint efforts of Russia and the United States.

At the request of the Russian government, USAID is terminating its overall program based in Russia. Thus, continuation of a significant U.S.-Russia bilateral effort to address HIV/AIDS in Russia is uncertain. Perhaps some aspects of USAID's global efforts will continue in Russia under the leadership of Russian counterparts.

3. *Responding to outbreaks of infectious diseases across international borders and containing their spread.* For many years, the U.S. Centers for Disease Control and Prevention (CDC) has teamed with a number of Russian institutions in responding to outbreaks of diseases in Russia and other areas that have had the potential for spreading across international borders. Particularly important training programs for Russian epidemiologists have been held, usually in Atlanta, Georgia. In 2012, CDC and the Federal Service for Surveillance on Consumer

Rights Protection and Human Well-being signed a Protocol of Intent of indefinite duration, which will continue joint efforts to address key concerns of the two governments to the extent that funding is available. (See Appendix C.6 for additional information on CDC collaboration with Russian partner organizations.)

An important example of collaborative efforts was the response to the outbreak of avian influenza in 2007, which is described in Box 5-3.

4. *Preserving biodiversity*. Both Russia and the United States have long histories of investigating the status of biodiversity resources throughout vast geographical areas, including areas outside their borders, such as tropical regions of South America and South Asia. Much of the interest of the two countries focuses on medicinal and food uses of plants that have been neglected in the past. An area of cooperation that has often been emphasized is inventorying species of concern and implementing practical steps to help prevent the near-term loss of important species. Activities of two key institutions in preserving biodiversity of global interest are set forth in Boxes 5-4 and 5-5.

5. *Addressing the scientific aspects of genetically modified organisms* (GMOs). This area is often plagued by arguments over health and environmental safety issues when formulating public policy. In 2010, the Russian Academy of Sciences and the National Academy of Sciences appointed a leading specialist from each of the two academies to prepare a joint assessment of the scientific basis for decision making concerning the ecological and food safety aspects of the introduction of GMOs in agriculture. A summary of that assessment is included

Box 5-3
Response to Outbreak of Avian Influenza, 2007

Russia is crossed by two major migratory flyways. Influenza A/H5N1 and other variants of avian influenza not previously found in Russia were isolated. There were two important tasks. Measures were taken to contain the spread of influenza A/H5N1, particularly through control of poultry. Research was initiated that quickly determined that one variant, influenza A/H4N6, had expanded its host range and that aquatic mammals, mainly muskrats, were involved in maintenance of the virus in nature. Russian specialists coordinated their efforts closely with related activities of U.S. specialists, particularly colleagues at CDC.

SOURCE: NRC, *Biological Research in Russia*, 2007, cited in Appendix A.2.

Box 5-4
Preservation of Botanical Resources

The herbarium and library of the V.L. Komarov Botanical Institute in St. Petersburg are among the world's most significant global botanical facilities, containing key specimens of plants not only from throughout the territory of the former Soviet Union but also from many areas of China and other Asian countries. The herbarium and library were repaired extensively with help from American colleagues in the early 1990s. As a result, they have maintained their status as world centers for botanical investigations, and their research materials are widely used. During the past decade, an extensive program of preparing digital images of critical specimens in the herbarium has been supported by the Andrew W. Mellon Foundation in New York. The institute will undoubtedly continue to provide an important site for facilitating cooperative botanical investigations.

SOURCE: V.L. Komarov Botanical Institute, September 2011.

Box 5-5
Maintaining a Repository for Agricultural Seeds

The N.I. Vavilov Institute of Plant Industry in St. Petersburg is a large repository for seeds of agricultural and scientific interest throughout the world. It preserves extensive samples of crop plants and their wild and weedy relatives while mounting expeditions in the former Soviet Union and beyond. The U.S. Department of Agriculture (USDA), which maintains a similar facility in Fort Collins, Colorado, has cooperated in many activities. For example, 60 Russian scientists from the Vavilov Institute, St. Petersburg State University, All-Russia Institute of Plant Protection, and USDA prepared an AgroAtlas that documents the distribution of 100 species of crop plants, 560 species of their relatives, and 640 species of crop pests, weeds, and diseases in Russia and neighboring states.

SOURCE: N.I. Vavilov Institute, 2011.

in Appendix F.4. The assessment can help officials and scientists worldwide to separate the scientific issues from the many other factors that influence decisions of governments concerning whether and under what circumstances to permit the use of this rapidly advancing technology. The academies have sent the scientific assessment to the International Research Council for consideration.

6. *Addressing polar interests.* Even during the darkest days of the cold war, U.S. and Soviet specialists worked together to investigate conditions in Antarctica and occasionally coordinated investigations in the Arctic region. Both the United States and Russia now support research programs in these polar areas, even in times of tight budgets. The Arctic Council provides an intergovernmental framework for addressing issues, such as search-and-rescue operations, responding to oil spills, and licensing of exploration activities that target natural resources. A variety of governmental and nongovernmental research centers in the United States, Russia, and elsewhere help coordinate biological research activities of various countries in the Arctic and in Antarctica.

Highlighted in Boxes 5-6 and 5-7 are two activities wherein U.S. and Russian scientists have played prominent roles.

7. *Carrying out joint efforts in third countries.* Both Russia and the United States have outreach programs to engage other countries in selected aspects of the biological sciences. Set forth in Boxes 5-8, 5-9, and 5-10 are examples of opportunities for the two countries to work together in supporting the development of biology-related activities in third countries.

Organizations that provide financial support for U.S. and Russian scientific efforts are increasingly aware of the rapid growth of global interests in biological research and biotechnology that have the potential for increasing the standard

Box 5-6
Circumpolar Scientific Observations in the Arctic

Building on a number of international projects carried out during the International Polar Year (2007–2009), the Arctic countries are now operating the Circumpolar Coastal Observatory Network with established reporting requirements. This network of institutions from all of the Arctic countries provides a framework for up-to-date observations of changes in the region due to climate shifts and more direct effects.

SOURCE: National Science Foundation, 2011.

Box 5-7
Assessing Effects of Black Carbon in the Arctic

Understanding and reducing the impacts of black carbon emissions that affect climate change and also the health of people in Arctic regions is a growing international concern. In response to the interest of the Arctic Council, the U.S. government has taken the initiative to engage Russian institutions in joint assessments of the emissions, circulation, and effects of black carbon. Inventories of sources, assessments of atmospheric transport and changes in the chemical composition of black carbon, and engineering approaches to mitigate emissions are among the many topics of interest. Current interest focuses on near-term assessments of the role of black carbon, with plans for long-term joint efforts in this field still evolving.

SOURCE: Department of State, March 2012.

Box 5-8
Eradicating Polio in Uzbekistan

Russian and American scientists played leading roles in the extensive efforts of the international community two decades ago to rid the world of polio. Unfortunately, polio still remains in small pockets of the world. The United States and Russia have committed to work together toward eradication of polio in Uzbekistan, although to date on-the-ground activities have been limited.

SOURCE: U.S.-Russia Protocol of Intent, 2011, and discussions with senior scientists in Russia, May 2012.

of living. Thus, in the years ahead, interest in bilateral cooperation on projects of global or regional significance should increase. Indeed, financial resources to support joint U.S.-Russian efforts may be more accessible if bilateral approaches to high-visibility topics are cast within a global framework, while retaining an emphasis on investigations of localized problems that are important components of overall international concerns.

Box 5-9
Enhancing Public Health Cooperation in Central Asia

The U.S. and Russian governments are interested in strengthening biological research capabilities of the countries of Central Asia, and most of these countries are currently expanding their research activities. With support from the international community, the countries are giving concomitant attention to biosafety procedures that are consistent with international standards that are evolving rapidly. U.S. and Russian biological scientists are beginning to work together in engaging counterparts in these countries. This is a useful step in establishing regional approaches that are carried out in a manner consistent with related efforts throughout the world.

SOURCE: Russian senior scientist participating in government-sponsored cooperation, May 2012.

Box 5-10
Global Fight against Malaria

In June 2012, the United States and Russia signed a Protocol of Intent to work together to help end preventable child deaths from malaria in Africa. Cooperation will entail training, capacity building, and operations research. The U.S. Centers for Disease Control and Prevention and the Russian Martsinovsky Institute of Medical Parasitology and Tropical Medicine will lead the effort.

SOURCE: U.S. Embassy, Moscow, June 2012, http://moscow.usembassy.gov/pr_062712.html.

CONCLUSIONS

Russian and U.S. institutions have worked well together in recent years in combating outbreaks of human and animal diseases, addressing the spread of health-threatening pollution that crosses international borders, and beginning the development of programs to adapt to climate change. Joint efforts to further strengthen the research, surveillance, institutional, and regulatory infrastructures in the two countries that can respond to these and other cross-border problems are important. Three conclusions in this regard follow:

1. *Coordination of research and development efforts to improve the diagnostic capabilities of regional and global disease surveillance systems can be significantly improved with only modest financial investments by both sides. Of particular interest is reducing delays and uncertainties in the international reporting of outbreaks within the framework of the International Health Regulations.*

The Russian government proposed a major initiative in express diagnostics in 2008 during preparations for the G-8 Summit in St. Petersburg. Unfortunately, other governments, including the U.S. government, were preoccupied with addressing issues concerning HIV/AIDS and tuberculosis, and they did not give the attention to the Russian proposal that it deserved. Nor have they given sufficient attention to the broadly based declaration concerning cooperation in disease surveillance that was adopted at the summit. Nevertheless, as both countries focus on upgrading their own diagnostics capabilities, progress in infectious disease surveillance that is relevant outside their borders is being recorded. Of particular importance is the need to reduce the times required to (a) recognize outbreaks that may cross international borders, (b) ascertain the causes of the outbreaks, (c) increase the number of disease agents that can be simultaneously detected and characterized, and (d) link detection and characterization determinations to global surveillance systems. These steps in turn contribute to efforts to constantly update assessments of global health conditions, relying on electronic networks that produce various types of up-to-date health maps of the world.

As an important example, growing interest in improved surveillance is reflected in the increasing investments in improving influenza test systems and diagnostic tools in both the United States and Russia. These efforts focus on many topics, including the following:

- Rapid influenza diagnostic tests, and particularly point-of-care diagnostics.
- Methods and materials for respiratory specimen collection.
- Respiratory pathogen tests on existing platforms.
- Advanced sequence detection methods for novel influenza strains.
- Identification of influenza strains that resist to antiviral drugs.
- Identification of influenza immunological response.

2. *The two governments are well positioned to assume broader regional leadership roles in their areas of special competence—independently and jointly—in addressing scientific challenges in the biological sciences. Central Asia and the Arctic are regions where joint efforts can pay off in the near term.*

The two governments have demonstrated that they can effectively work together, in cooperation with local authorities, in addressing broad public health and related biosafety issues throughout Central Asia. Both countries have extensive contacts in the region. Specialists from both countries are respected for their competence in the biological arena. Joint efforts can forge relationships between

Russian and American specialists while also developing coherence of approaches within the region.

As to the Arctic, many common concerns provide a strong basis for cooperation in the area near the Bering Straits. Also, as climate change increasingly is recorded across the Arctic, the opportunities for expanding cooperation along the northern coastline of Russia are particularly important. Of special interest are technologies for effectively and economically converting biomass to new sources of energy, thereby reducing reliance on coal and other heavy polluting energy sources in snow-covered regions.

3. *The two governments have made a good start in joint efforts to limit the spread of tuberculosis and other devastating diseases in Russia and neighboring areas.*

An important framework for promoting joint research and development efforts devoted to multidrug-resistant tuberculosis and other difficult diseases was established in November 2011, with a forum in Moscow involving key agencies from the two countries. The U.S. private sector also played an unusually active role in promoting cooperation. The seriousness of many of the problems in Russia—and indeed throughout the world—is widely recognized. Now there is a considerable need for more aggressive collaborative research efforts. (See Appendix F.5.)

6

Impacts of Bilateral Programs and Projects

This chapter provides an overview of important returns on the investments by the two countries in bioengagement. The investments have involved many research and development institutions and associated facilities where scientists from the two countries have worked together. As we have seen in previous chapters, a variety of applications of existing knowledge and technologies have helped responses to social and economic needs as well as improving understanding of the underlying science. These achievements have been taking place as the security, political, and economic architectures of the world have been undergoing dramatic changes.

U.S.-Russian bioengagement in recent years has been unique among bilateral and multilateral relationships in the life sciences throughout the world. The breadth of bilateral objectives, the variety of field and laboratory endeavors spread over vast land and aquatic areas, and the diversity of well-honed skills of participating scientists in bioengagement have been unrivaled. The transition from an era of hostility and isolation to an era of political rapprochement and scientific cooperation has no historical precedents, with bioengagement near the center of this transition.

For decades biology-related issues were a significant, and at times a highly contentious, component of adversarial U.S.-Soviet confrontations concerning appropriate directions of scientific expertise and facilities. Suspicions were rampant, fueled by allegations of concealed activities at biological research centers in both countries. Overall, collaborative endeavors were limited in scope and number.

But beginning in the mid-1990s, biological challenges have become a nexus for mobilizing U.S. and Russian capabilities based on common interests in enhancement of health, agriculture, and environmental conditions while reducing security apprehensions. This transition to openness and cooperation, while still incomplete, and the associated development of long-term professional and personal relationships across borders have been quite remarkable.

In recent years, the two countries have been on parallel paths to develop their capabilities in the biological sciences and biotechnology. They are giving special attention to enhancing research capabilities of universities and other scientific centers and expanding industrial efforts to provide new biotechnology products and services. At the same time, they are encouraging entrepreneurial endeavors of young and energetic entrants into the field of biology, who increasingly populate the research institutions of the two countries.

Of course, the paths of the two countries aimed at successful development and use of biological assets are far from identical. The different starting points vividly stand out when comparing the (a) international rankings of university laboratories and (b) different experiences in commercialization of biotechnology products. In both areas, U.S. biological accomplishments are much higher on the scales of achievements. But still, the paths of the two countries often cross as the governments and nongovernmental institutions support different types of engagement, ranging from large intergovernmental projects of broad political as well as scientific interest to people-to-people contacts based on common professional experiences of individual specialists.

In recent efforts to catch up with other industrialized countries, Russia has been slowly increasing support for basic research in the life sciences, particularly in the universities where they have lagged far behind. At the same time, the government is investing relatively large sums of money in applied activities as discussed in Appendixes E.3, E.5, and F.3. These trends should enhance opportunities for mutually beneficial U.S.-Russian interactions.

OUTCOMES OF COLLABORATION

In the area of national security, U.S. financial support during the 1990s and early 2000s of Russian endeavors to enhance biosecurity and biosafety approaches and capabilities substantially reduced the risks associated with possible misuse by malcontents of the biological assets of Russia. As an important component of this effort, the United States joined with Russia in supporting redirection of thousands of underemployed Russian scientists in the defense sector to jobs in the civilian sector that provided pay supplements during economic downturns in the country. The joint activities have also upgraded the equipment bases and related infrastructure weaknesses of Russian research institutions, which then have hosted redirection activities. And at times, the programs have responded in a modest way to the Russian government's near-term priorities for development of saleable products and services, which in turn help with self-financing of research activities.

Scientific advances that can be attributed at least in part to cooperation are still unfolding. But some progress seems clear, as exemplified by the results of completed projects and related activities set forth in previous chapters and in the appendixes. Of most importance, new international networks among scientists have been established and are being maintained, thereby enhancing coordination of related research endeavors. International travel of scientists to conferences in the two countries has become more frequent. A number of Russian-authored and coauthored international journal articles can be attributed in part to bilateral scientific engagement; indeed, publications should be an important outcome of some types of collaboration. (See Appendix F.1 for the state of joint publications that reflects the need for Russia to give more emphasis to publication of research results.) And at the core of the important results of bioengagement are (a) hundreds of scientists in the two countries who know colleagues across the ocean and remember their positive experiences in working with them in cooperative projects, and (b) the legacy of highly productive institutional cooperation, such as the partnerships that developed between the institutions affiliated with the Agricultural Research Service of the United States and a number of agricultural research centers in Russia.

An important aspect of international exchanges has been opportunities for scientists of one country to become acquainted with research techniques and accomplishments of colleagues in the other country. Onsite interactions have improved appreciation of the significance of articles that have been published by colleagues in national and international journals and of the potential of experiments described in unpublished documents. Such first-hand insights are of particular importance in looking to the future when biological breakthroughs may depend on adjustments in investigative techniques, particularly adjustments that are in their preliminary stages of exploration by international colleagues.

With regard to applications of scientific capabilities in the private sector, many commercialization efforts in Russia have been disappointing. This is not surprising, given the difficulties in the United States and other countries with well-developed market economies in transforming research results into saleable products. However, cooperative efforts to encourage the development of products and services that will attract customers have been important in the education of potential high-technology entrepreneurs in Russia. Research management within a market economy has not been a familiar topic within Russia, and collaborations have often been important introductions to the necessary adjustments of previous management styles.

U.S. counterparts have benefited from the technical contributions of Russian researchers to joint efforts. But if near-term sales of new products are used as the only metric for assessing the payoff from applied research activities, collaborative programs have fallen short. However, in the long run, it is often the educational process for entrepreneurs that will lead to the most important yet-to-be measured outcomes; and the results of this educational process are being increasingly reflected in the activities of some research institutions in Russia.

Finally, with regard to regional and global impacts of joint efforts, neither country has been hesitant in encouraging appropriate dissemination of the results of joint projects to other countries. Perhaps the most dramatic example has been the global diffusion of space biology, which was developed through parallel and joint efforts of the USSR-Russia and the United States, as discussed in Chapter 5. Also, the two countries have participated in investigations of remote polar and desert areas, leading to discoveries that help predict future environmental conditions around the globe.

Highly visible U.S.-Russian efforts in the biological sciences, particularly those championed by the International Science and Technology Center, have attracted attention of important international organizations, including the Global Partnership initiated by the G-8 countries. These countries have welcomed approaches pioneered by the United States and Russia in the biological sciences as having worldwide implications. They have encouraged the two countries to continue their efforts, particularly in promoting responsible use of technologies that could be diverted for inappropriate purposes.

Measuring, or even cataloging, many of the results of joint efforts is not possible. Some new developments will become clear, only in future years. And the economic and social benefits from scientific discoveries may not be realized for decades. (See Appendix C.2 for one example of indicators of success that have been used in assessing the near-term results of cooperative biosecurity programs in Russia.)

ELABORATION OF SELECTED OUTCOMES

Against this background, eight types of outcomes are discussed below.

1. *Enhanced access by foreign scientists to previously closed or isolated institutions in the two countries.* Many participating institutions and scientists in bilateral programs have been relative newcomers to U.S.–Soviet-Russian cooperation. They were previously constrained from reaching out by security concerns, by lack of financial resources, or by lack of appropriate information about institutions of potential interest.

With official encouragement to engage foreign colleagues whom were known only through their publications or, in many cases, were not known at all, hundreds of scientists in the two countries have had opportunities to assess first-hand the capabilities of counterparts, and thereby better appreciate the importance of their work. Most of the visits have taken American specialists to Russia, although reciprocal visits have been frequent. At the same time, scientists from abroad often have been reassured through personal observations in the partner country that previous concerns about potentially dangerous activities in foreign laboratories were no longer real concerns, even if they had in earlier times been identified as questionable undertakings. Through scientist-to-scientist engagement, understanding and trust have often replaced suspicion and apprehension with transparency being an essential component of personal contacts.

A good example of opportunities in this area is the recent interest on both sides in establishing long-term contacts between specialists of the U.S. Agricultural Research Service and their colleagues at the agricultural research center in Pokrov in Russia. The current dialogue followed several years of discussions about mutual interests. Unfortunately, during the long delay, the economic condition at Pokrov has deteriorated; but new collaborative projects could assist in revitalizing important scientific capabilities.

2. *The transformation of a foreign assistance relationship between the United States and Russia to a series of mutually beneficial partnerships.* Too often in the 1990s, the United States provided simply research funds for joint projects while Russia provided most of the scientific brainpower. This form of cooperation resulted at times in very useful research findings but greatly distorted the traditions of science. Reliance on a donor-recipient relationship was destined to have a short lifetime.

First in the nuclear area, and then in the biological sector, the Russian government gradually assumed responsibility for financing a greater share of joint research and related activities. This transition is still in its early stages. But as the funding responsibility began to change, the attitudes of the participants also changed in a positive direction. The biologists have played an important role in the effort to transform scientific "assistance" to more lasting partnership arrangements, with the potential to continue in the future.

3. *Facilitation of the recovery of decimated Russian research groups to financially viable research teams, which effectively complemented U.S. and other international research capabilities.* The financial plight of many Russian biological research centers during the 1990s was desperate. Staff departures were commonplace, and the entry of young biologists into the labor force was minimal. Support programs that were quickly developed by the U.S. government and by private foundations in the United States provided critical lifelines. This effort enabled many highly talented researchers to remain in place until increased financial support of science by the Russian government began to preserve premier scientific establishments and replenish the cadres of promising young scientists.

4. *Strengthening capabilities in both countries to prevent, detect, diagnose, and control outbreaks of dangerous infectious diseases.* For several years beginning in the late 1990s, an important emphasis of joint programs was research on a few diseases that had been previously given special importance in defense programs—for example, anthrax. The scientific achievements in improving

understanding as to how to deal with such pathogens through collaborative research efforts were important. In time, the list of potent pathogens of mutual concern that were considered in cooperative endeavors expanded significantly. Russian and American investigators earned recognition as leaders in addressing dangerous pathogens, including pathogens that had little relevance to defense applications. Their findings encouraged the strengthening of global capabilities to deal with the threats posed by a large number of dangerous pathogens, including naturally occurring pathogens of day-to-day concern of health officials.

Most health officials, at least in Russia, consider preventing deliberate misuse of biological assets to be a less urgent task than servicing day-to-day public health needs of the general population. At times, the lists of pathogens of priority concern to the U.S. government focused only on pathogens that had been categorized as "especially dangerous" by the Department of Defense. But within a few years, there was common recognition that health systems must focus on a range of pathogens, including pathogens far from defense concerns, if many countries were to be interested in upgrading their surveillance systems.

5. *Demonstrations of cost-effective approaches to improving biosafety and biosecurity on a national scale.* In the 1990s, joint U.S.-Russian efforts to ensure that biological assets would be used responsibly attracted considerable international attention. With these bilateral efforts leading the way, soon other countries had joined in international programs to upgrade their biosafety and biosecurity requirements and processes for conducting biological research. In particular, a number of countries that were part of the former Soviet Union are using the approaches refined through U.S.-Russian programs as models to be emulated.

6. *Demonstration of feasible approaches to bringing the products of biotechnology to market in an economy undergoing dramatic reconfiguration.* The United States has sought greater attention by the Russian government to the development of small and medium firms, which can transform the results of research into marketable products. While the payoffs from joint efforts to commercialize the products of research carried out in Russia have been limited to date, the two countries are now well attuned to the realities of commercialization of technology and the important roles that both small spin-off firms and joint ventures can play in this regard.

There have been limited Russian success stories in establishing small biotech firms, which have helped illuminate the best paths to financial returns from innovations in the field of biotechnology. Of special interest is the marketing of products that were developed for Russian consumers as a first step toward entering international markets. See Appendix C.3 for a number of examples of modest commercial successes.

7. *Increased national, bilateral, and multilateral cooperation focused on*

research activities at selected Russian universities. Immediately following the breakup of the USSR, Russian academics and scientists began a clamor for greater attention to strengthening research capabilities at Russian universities. However, financial resources were not available. With considerable support from the U.S. university community and limited financial support from U.S. foundations, a few model programs were launched to expand research at Russian universities. Also, following another U.S. model, medical faculties with both educational and research agendas were established at several leading Russian universities. Building on this experience and other activities financed by the Russian Ministry of Education and Science, the Russian government has designated 29 universities as "research universities" and has supported a variety of international research partnerships involving these universities—some on a bilateral basis with the United States and others on a broader international basis. These universities in Russia seem destined to become a significant dimension of the overall international outreach effort in the life sciences, as well as in other fields.

8. *Increased international interest in the importance of biodiversity and practical steps to catalog and preserve biodiversity.* Both Russia and the United States are treasure troves of animal, insect, and plant species that have been of broad international interest. Programs to help preserve biodiversity, while recognized internationally as being important for all countries, have considerable difficulty attracting financial support beyond base budgets needed to keep scientific institutions active. With the economic crisis in Russia, special efforts were needed to raise the profile of these activities and to document the importance of past findings and future opportunities in this field. Joint work by institutions in the two countries played an important role in ensuring that collections of plants, seeds, and animals—unique in the world—were maintained even in the most difficult economic times.

FUTURE OPPORTUNITIES

In summary, the recent joint achievements of two former adversaries are many fold. Partner organizations have sponsored important research activities at sensitive facilities and remote field sites and also maintained long-standing cooperative activities in scientific areas distant from dual-use or other types of security concerns. The two countries have brought to the table both common and different assets and aspirations in the biological sciences that can continue to provide strong platforms for joint efforts. The lessons that they have learned during development and implementation of a wide variety of programs are of considerable value to other organizations interested in cooperative efforts in a variety of political settings. In short, the bilateral relationship has led to significant rewards for the global community in the past and can continue to set a rapid pace in advancing responsible biological science activities in the future.

Skeptical officials and scientific leaders of the two countries, who initially questioned the feasibility and acceptability of a broadly based engagement approach, have developed respect for skills of counterparts in dealing with sensitive technologies. In a brief period of time, responsible development, handling, and use of potentially dangerous technologies have become cornerstones of these efforts. Of particular importance, the increased transparency of programs in sensitive areas, directly related to broad access to facilities and specialists in the two countries, has set the stage for still more important cooperative ventures that could contribute to science and security interests throughout the world.

A good indicator of the immediate importance of bioengagement is the role that biological activities play within the framework of the Bilateral Presidential Commission established by the two governments in 2009. With six working groups addressing various aspects of the life sciences, the list of recent activities is long despite the limited budgets available to carry out such activities. (See Appendix E.1.) During the 8-year period from 2001 to 2009, when there was no Bilateral Presidential Commission but budgetary resources were more plentiful—at least on the U.S. side—the importance of such activities never wavered. In 2012, the situation is dramatically different with availability of funding a major constraint, and gradually bioengagement is falling off the screen of viable activities.

THE ROLE OF METRICS

Chapter 1 concludes that bioengagement is undervalued and notes that subsequent chapters document many of the successes to date. But good metrics for assessing success are lacking. Therefore, *greater attention to developing and using metrics in designing and evaluating program results, with particular attention to long-term results and the characteristics of programs that contribute to continued viability of research teams, can be helpful in determining the importance of bioengagement activities.*

In short, more deliberate efforts to build into future bioengagement programs methodologies for evaluating the results of these programs for scientific advancements, applications of science to economic development, and progress in achieving common security and foreign policy goals could (a) help focus implementation activities more sharply on key bioengagement objectives and (b) highlight the payoffs from even modest investments in bioengagement.

Efforts in Washington to develop metrics for assessments of bioengagement activities have given little attention to metrics that will indicate the extent to which projects lead to long-term success in building effective research teams. Rather, too often metrics have focused only on near-term security concerns. Important results of future cooperation help build capacities in the two countries, and indeed globally, in order to promote responsible science. Adoption of responsible approaches to research and applications should be a key factor in determining success of activities.

7

Impediments in Carrying Out Approved and Funded Collaborative Projects

Government agencies, universities, research institutions, private-sector companies, and individual scientists in the United States and Russia have derived many benefits for both countries and for individual participants through bioengagement projects. At the same time, however, these institutions and individuals have often encountered operational impediments that have complicated implementation of activities after project approval at appropriate levels of the governments, as well as by the leaders of the institutions that are involved.

OVERVIEW OF DIFFICULTIES

Issues surrounding visas, taxes, customs duties, money transfers, financial accountability, access to geographic areas and facilities, and transfer of biological samples, for example, persist despite repeated efforts by the governments to resolve difficulties. At times, the two governments have taken the initiative to resolve problems that have arisen during implementation of projects. But more often, the institutions responsible for program implementation and the individual project participants have assumed the responsibility for finding ways to overcome barriers.

Most difficulties hindering bioengagement also permeate cooperation in other fields of science. In particular, government agencies in the two countries have often singled out proposed "science" exchanges for special visa and other types of reviews, resulting in delays and complications. A common reason for such reviews of applications from participants in science programs is the possible linkage of proposed activities with export-control regulations or with other security concerns.

Generally, however, working together in science has broad appeal in both countries. Joint scientific efforts, and of course joint successes, frequently engender strong support from the general public as well as the governments. Development and implementation of science programs are usually less controversial politically than exchanges in some other areas. Also, programs that provide for large financial transactions across international borders are usually scrutinized carefully by authorities in the two countries.

Difficulties that arise during implementation of cooperative science projects depend in large measure on the extent and depth of the preparatory steps to carry out different types of activities. Such advanced planning is particularly important if the activities involve collaborators at institutions that have little experience in receiving foreign visitors. Also, arranging visits to geographical areas that are not on traditional itineraries of foreign visitors may be difficult for inexperienced hosts.

Usually, activities explicitly endorsed in documents issued by appropriate government agencies in the two countries before they begin encounter fewer administrative delays than activities that are arranged without such official support. But sometimes difficulties even arise in carrying out projects that are considered "priority" efforts by the sponsoring government agencies. Nongovernmental programs involving access to sensitive information or facilities that are not completely open are particularly susceptible to unanticipated disruptions by local officials who are unaware of itineraries approved in Moscow or Washington.

For many years, the two governments have relied on one or more intergovernmental working groups to encourage removal of unwarranted impediments to cooperation. The working group that addresses most of the "routine" problems inhibiting cooperation in the life sciences works within the framework of the Agreement on Science and Technology Cooperation. The focus has been primarily on impediments that delay government-sponsored activities. However, at times the working group has considered issues that have significant effects on the interests of the private sector as well, with the exception of trade relations, which are usually handled in other forums.

This chapter highlights several issues that have been of interest to the intergovernmental working group. These issues are (a) delays in issuing visas along with travel and time limitations associated with Russian visas, (b) customs duties levied on imports of scientific equipment, (c) tax status of international and foreign research organizations operating in Russia, and (d) delays in obtaining authorization for marine scientific research. While the working group has been an important focal point for addressing these topics, the issues are also discussed in other venues, such as meetings between embassy representatives and officials of the Department of State (in Washington) or the Foreign Ministry (in Moscow).

The chapter also considers (a) ownership of intellectual property (IP) that is developed through cooperative activities, and protection of existing IP that is exposed during collaboration; (b) access by participants in joint projects from one country to sensitive facilities in the other country; and (c) exchanges of biological material, including strains of pathogens.

Before addressing the foregoing issues, the importance of having access to reliable funding for carrying out both planning activities and implementation activities should be underlined. **Without funding for cooperative activities, there is little motivation to be concerned about impediments that seem abstract.**

VISAS

Delays in issuing visas and the short lengths of stay that are often permitted by visas have for many years been barriers to more extensive U.S.-Russian cooperation in scientific research and in other science-oriented activities. In July 2012, agreement was reached on a new bilateral visa agreement between the two countries that then entered into effect in September 2012. The agreement provides for multiple-entry visas with a validity of 36 months for most business and tourist visitors. Official visitors are to have 1-year multiple-entry visas. If long-term visas are issued for cooperative science programs, they should resolve a number of the visa problems associated with bioengagement. Of course, visa officials may decide that 3-year visas are not appropriate for certain activities, and there undoubtedly will be continuing issues surrounding the issuance of visas.

One visa-related factor that the governments consider is the linkage of biology to terrorism and proliferation concerns. According to reports in 2012 from Russian scientists who applied for American visas, visa applications that include the words "molecular biology," "virology," or "immunology" may be subjected to special security screening in Washington, with attendant delays. If true, U.S. authorities have taken unnecessarily extreme measures that inhibit bioengagement.

Until 2012, the limited time allowed in Russia to a visitor who was conducting research (a maximum of 90 days during a single 180-day period) hindered efforts of some researchers in completing their activities on schedule. Also, clarification of procedures for American scientists to obtain permission to conduct research near international borders, particularly in outlying regions of Russia that have different access requirements from region to region, would have helped foster exchanges when travel to certain geographic landscapes was important. It is too early to know whether the new visa regime will significantly reduce such problems.

As to U.S. policies and practices, delays in issuance of visas have at times prevented Russian researchers arriving on schedule for international conferences and other events. By 2012, the time required for issuing U.S. visas to Russian scientists had been reduced, on average, to about 3 weeks. But in some cases, the delays were unacceptably long. The process is often burdensome for Russian scientists who do not live in Moscow, St. Petersburg, Yekaterinburg, or Vladivostok, where U.S. visas are issued. The travel from Russian towns to far-away U.S. consulates to apply for or to pick up visas may be difficult and expensive, and last-minute arrangements to pick up visas sometimes are not possible. Also, reliable and expedited delivery services are not available in many towns of Russia.

As is well known, each visa applicant must take personal responsibility for allowing sufficient lead time for issuance of the visa, in accordance with requirements set forth by each government. While both governments continue efforts to expedite issuance of visas, they should also give attention to ensuring that potential visa applicants are adequately informed as to the time needed for processing visa applications and as to the status of applications. There have been frequent changes in procedures in recent years, and at any given time, applicants may not be aware of the latest requirements.

CUSTOMS DUTIES LEVIED ON SCIENTIFIC EQUIPMENT

At present, each side is obligated to "facilitate" imports of equipment to be used in many agreed bilateral science projects. But "facilitate" apparently does not mean that the customs duties must be waived. In short, the payment of customs duties has been and remains a difficult issue in carrying out projects within the framework of the Agreement on Science and Technology Cooperation.

For many years, the International Science and Technology Center (ISTC) has facilitated the entry into Russia of scientific equipment associated with ISTC projects, with the customs fees waived. At times, there have been misunderstandings at the Russian port of entry concerning the extent of the authority granted to the ISTC. But in general, ISTC facilitative services have been quite effective.

However, the ISTC has retained the titles to the imported equipment that has been financed by ISTC parties and partners. Now, as the ISTC prepares to cease operations in Russia in 2015, tax-free transfers of the titles that the ISTC currently holds to the Russian research centers where the items are located has become a significant issue.

Also, since the late 1990s, the Civilian Research and Development Foundation (CRDF) has offered a service to expedite imports of scientific equipment into Russia. Customs charges have been a continuing issue. At present these charges cannot be avoided. Also, CRDF charges a modest fee for its facilitative services.

It is not surprising that many U.S. and Russian collaborators have relied on the ISTC and CRDF to help with the transfers of scientific equipment. However, with the withdrawal of Russia from the ISTC and uncertainty as to the long-term status of CRDF in Russia, transfer of equipment will undoubtedly be an issue of concern. But if the two countries move toward a new model for cooperation that provides for each side to support its own scientists, transfers of money for equipment, salaries, and other purposes should be less frequent.

During the early 2000s, the availability of foreign scientific equipment for sale by Russian importers increased significantly. For foreign-made equipment, customs duties are included in the sales prices. The availability of foreign equipment in the sales departments of many large Russian companies, together with the maintenance service provided by Russian-based technical representatives of the manufacturers of the equipment, has reduced the need for Russian institutions to arrange their own imports of equipment. They can now buy equipment at sales outlets in Russia. Of course, the prices may be significantly higher than equipment imported through the good offices of the ISTC or CRDF.

Some advanced technology items are not available in Russia. Often, special imports must be arranged at considerable cost; and as previously noted there is not agreement that obligations to "facilitate" items through customs, means duty-free entry. As a specific example, several scientists associated with the U.S. Fish and Wildlife Service terminated their cooperation with Russian colleagues because it became too time-consuming to obtain permission to work effectively across international borders. A significant problem involved imports of global positioning system devices and satellite tags used in animal migration studies. Some marine mammals and birds of interest that migrate between Alaska and Chukhotka have the potential to spread different types of diseases, such as avian influenza, that could then be transmitted to human populations.

TAX STATUS OF U.S. RESEARCH ORGANIZATIONS OPERATING IN RUSSIA

In 2009, the Russian government removed all but 12 international and foreign organizations from the list of organizations entitled to provide tax-free grants to Russian recipients. Most of these 12 (now 13) organizations are U.N. and European regional organizations. The Russian Ministry of Finance was to develop procedures for reinstating many of the other organizations and adding still others to the tax-exempt list on a regular basis, but this has not occurred. The Duma has been considering legislation that would grant additional foreign and international organizations tax-exempt status.

This issue affects the activities of U.S. government agencies, such as the Department of Energy, and nongovernmental organizations, such as CRDF, which have been on and off various lists. The intergovernmental working group is attempting to have the Ministry of Finance include on the list a number of U.S. organizations involved in cooperative programs that would receive favorable tax treatment, similar to that accorded to Russian-European scientific cooperation.

In summary, tax aspects, along with customs requirements, clearly deserve special attention, including appropriate budgeting for expenditures to meet legal requirements. Legal issues often require expert opinions that should be obtained prior to undertaking joint efforts, so that surprises during implementation are avoided. The governments can play helpful roles in these areas.

MARINE SCIENTIFIC RESEARCH

Both the United States and Russia have research vessels with long-distance cruising capabilities. The United States has consistently been slow in granting permission for Russian vessels to operate close to the U.S. shoreline. At the same time, delayed Russian authorizations can cost the United States up to $40,000 per day of delay in carrying out fisheries-related research near Russian borders.

An example provided by the Department of State of the problems with permission to enter waters close to Russia is as follows:

> In 2011, scientists associated with the Russian-U.S. Long-term Census of the Arctic research program on board the Russian-flagged vessel *Khromov* were prevented by the Russian navy from entering Russian territorial waters to retrieve three oceanographic moorings. These moorings had limited battery time. Some of the data will never be retrieved. It is clear that this administrative problem could have been avoided through better communications, and it harmed the carrying out of a costly Arctic research program that has significant biology-related components.

The situation apparently improved in 2012.

LEGAL BASIS FOR ACTIVITIES

Appropriate documents signed by authorized government officials or institutional leaders in both countries are often needed to conduct cooperative scientific activities abroad. These documents may be intergovernmental agreements, memoranda of understanding, or simply exchanges of letters. Whatever the format, they are important. And they must have the correct stamps and signatures. Even the best-designed joint activities can be disrupted through lack of appropriate and readily available documentation.

INTELLECTUAL PROPERTY RIGHTS

Financial benefits to be derived from protecting IP and the procedures for obtaining patent or copyright protection are often poorly understood by inventors of technological innovations. Occasionally, IP rights have been a contentious issue in setting the stage for a cooperative activity. At times, patent protection may be critical for successful marketing of products.

However, the significance of patent protection may be exaggerated. In Russia, in particular, an inventor may be more interested in having a patent certificate to hang on the wall than using a patent as an incentive for a paying customer to adopt a new discovery. The inventor may have witnessed too many colleagues waste their time searching for customers, although at the same time the inventor would like personal recognition for his or her technical achievement.

Nevertheless, the lack of agreement on such protection can inhibit sharing of information. Also, such a situation can deny an inventor of a fair share of the income that is received from unconstrained use of information, which should belong to the inventor. This is particularly important when newly developed advanced technologies are integral to the successful completion of collaborative projects. Further complicating the situation is distinguishing new technological approaches—approaches that presumably are governed by contractual arrangements—and utilization of old technological discoveries, which presumably belong to the institution that had developed the technologies before entering into a contract.

More than a decade ago, the U.S. government decided to incorporate a standard IP clause in each relevant agreement signed by the two governments. The idea was to be sure that all parties agreed in advance as to how successful endeavors were to be handled. But the approach throughout the U.S. government is not completely standardized. Agencies have the flexibility to determine in negotiations with foreign partners the ownership aspects of discoveries resulting from a grant or contract that they are prepared to award.

Also highlighting differences in approaches, the U.S. Agency for International Development (USAID) has used the common foreign assistance practice of granting to recipients of assistance all IP rights for using results of activities that are carried out through joint efforts. This practice reflects the very purpose of USAID. It was established to be an assistance agency, not a promoter of U.S. commercial interests in the first instance.

The ISTC has had a different approach. Russian recipients of ISTC funds provided by the United States obtains exclusive IP rights within Russia for technologies that are developed. A U.S. collaborating organization has exclusive IP rights within the United States. The rights in other countries are divided on a case-by-case basis. However, the ISTC also has an exception clause, which permits the donor and recipient to decide for themselves how the rights are to be divided. This exception has often resulted in most, if not all, of the rights for products resulting from U.S. government investments going to collaborating U.S. institutions identified by the U.S. government.

Also of importance is the protection of IP belonging to U.S. organizations that is exposed during collaborative activities. The only enforcement mechanism in preventing the unauthorized use of IP belonging to U.S. organizations is the Russian court system, which in principle can resolve complaints of owners of IP who contend that others have used their IP without appropriate compensation. But the courts have little experience in this area, and demonstrating for perhaps the first time that a partner has unfairly used previously patented innovations may not be simple.

INTERNATIONAL TRANSFER OF FUNDS

The international transfer of funds—in the past primarily from the United States to Russia—to support project activities has sometimes been complicated. There may be tax issues, delivery issues, and privacy issues. Of course, the best situation is for each side to cover its own expenses, avoiding the necessity of international fund transfers. However, there may be financial, programmatic, or other reasons for not following this general rule.

As previously noted, the ISTC has been an important mechanism in avoiding problems with fund transfers to Russia. CRDF has also been important in this regard. However, some organizations have not used these services—relying on commercial channels or other approaches. They have at times encountered difficulties ranging from (a) lack of preparedness of Russian institutions to accept such transfers in an acceptable manner to (b) misuse of funds due to lack of financial transparency and inadequate accountability.

Looking forward, collaborating institutions are increasingly arranging for fund transfers, when necessary, through normal banking channels. This approach will surely help develop U.S.-Russian relationships that are consistent with international practice.

SECRECY, CLOSED FACILITIES, AND SENSITIVE INFORMATION

In the 1990s, the launching of bilateral programs, particularly those motivated by concerns over proliferation of sensitive expertise or dangerous materials, often encountered difficulties with attempts to (a) open closed facilities to foreign visitors to discuss joint projects and (b) discuss details of projects linked to security issues. These problems gradually declined, although they never completely disappeared. Indeed, for security reasons, some facilities in both countries remain closed to outside visitors. And some topics are simply off limits for serious discussion.

The situation in the field of biology and biotechnology was particularly difficult during the 1990s, given the history of mistrust during early efforts (the trilateral visits involving Russia, the United States, and England designed to resolve concerns over compliance with the Biological and Toxin Weapons Convention) to verify that prohibited activities had come to an end. Then as facilities began to open, mutual trust slowly evolved, although access was often denied to certain areas of facilities that had been heralded as open to international visitors. Nevertheless, the degree of openness is quite extraordinary in view of the contentious history of the relationship in this field. The cooperative projects set forth in Appendixes C.2, C.3, and C.4 are impressive evidence of the international transparency that has developed at sensitive Russian research centers working with U.S. centers.

Also, dissemination of information concerning specific project activities has often raised issues. Of particular concern have been information exchanges that could be viewed as impinging on (a) state secrets, (b) protection of IP, or (c) rights of individual researchers to claim credit in publications for their scientific findings. At other times, uneasiness has arisen over the possible embarrassment of managers if outsiders visited deteriorated facilities that had not been refurbished due to lack of financial resources. Generally, these problems are now of less importance than in years past, as collaborating scientists have become accustomed to a new style of openness.

EXCHANGES OF BIOLOGICAL MATERIALS

Difficulty may arise when researchers attempt to send biological materials or chemicals used in biological experiments into countries where collaborators reside and to receive materials from these collaborators under exchange commitments. Each country has limitations on shipments of certain types of material, with these limitations often linked to international export control obligations. In addition, individual ministries and departments may have their own restrictions. But at times, there is some flexibility in administering these limitations.

Details are important, particularly when dealing with dangerous pathogens. Institutions that send or receive materials may have even more stringent requirements than formally required and complicated approval processes. Shipping companies may be constrained in their activities, by national laws and by their own internal procedures. There may be requirements as to shipping containers.

A particularly contentious issue during the early 2000s was the insistence of the Department of Defense (DOD) on shipment of strains of sensitive biological pathogens from Russian research centers to the United States as a condition of providing support for U.S.-financed activities in Russia. The Russian side contended that its export controls had been imposed in response to pressure from the United States to limit the shipping of strains abroad. Also, DOD was not prepared to send other strains of interest to Russia in exchange. This issue was never adequately resolved, and the discussions delayed implementation of several projects.

Finally, it is important to note that not all difficulties with exchanges of biological materials have involved sensitive strains. For example, the U.S. National Park Service has encountered difficulties in transferring biological samples involving marine mammals and Beringian flora and fauna to the United States. Also, scientists supported by the National Science Foundation have had difficulties obtaining botanical samples from the Tiksi research station in the northern area of Russia.

CONTINUING EMPHASIS ON REDUCING IMPEDIMENTS

Against this panorama of technical barriers to cooperation, the impediment to bioengagement that is most commonly cited by program participants is the delay in issuing visas. Other concerns also deserve attention. Thus, the committee underscores the following four conclusions:

1. *Reducing the time and difficulties associated with the issuance of visas for participants in cooperative activities is very important for effective bioengagement.*
2. *The working group on impediments (now referred to as working group on enhancing cooperation) under the Agreement on Science and Technology Cooperation has played an important role in efforts to reduce obstacles that inhibit the implementation of bioengagement activities.*
3. *During development of new or expanded cooperative programs and projects, the possibility of impediments limiting activities deserves careful attention.*
4. *Careful documentation of the experience of the ISTC in addressing impediments can be very helpful to government agencies and other institutions interested in future collaboration. This report is a step in this direction.*

8

Lessons Learned

What are the best approaches for formulating and agreeing on common objectives at both the program and project levels for bioengagement activities? In the planning of joint programs for implementation in an uncertain financial environment, what types of early steps should be considered to increase the likelihood of continuation of successful activities, even in the absence of special funding for follow-on activities? How can projects that are not producing anticipated results be terminated without creating animosities that could jeopardize future endeavors?

These are but three of the many questions that confront managers of U.S.-Russian bilateral programs as they begin to put in place and then carry out joint activities. Failure to address such issues in a timely manner can reduce the likelihood that cooperation will lead to useful results. In particular, even if administrative arrangements for initial research activities seem flawless, the activities may have little effect on scientific or economic advancement or security enhancement in the absence of early identification of feasible approaches for capitalizing on research achievements.

Views of program sponsors and of participants in recent bilateral activities, as well as comments by close observers of bioengagement activities, provide insights that are useful in seeking answers to such questions. The personal experiences of members of the committee responsible for this report, together with observations of other participants in joint activities, are the basis for the comments that follow.

INTERESTS AT THE POLICY AND INSTITUTIONAL LEVELS IN LESSONS LEARNED

Lessons learned from past activities should be of interest at the governmental and institutional levels, and 10 are set forth below. In the subsequent section of this chapter, lessons of special interest to individual researchers are presented.

1. As previously noted, during the 1990s, U.S.-Russian cooperation in the life sciences and in many other fields was, in a number of ways, a foreign assistance relationship. In recent years, however, scientific cooperation between the two countries has been slowly transforming into a series of partnerships, with both sides playing active roles in planning projects, in providing financing, and in sharing results and benefits from activities. Equitable sharing of direct costs of cooperative programs has been a particularly difficult issue, given the precedent of earlier patterns of U.S. organizations providing most of the financial support to cover direct costs.

The Russian government has gradually increased its contributions to joint efforts. Despite this positive trend, at times U.S. counterparts who have been accustomed to controlling the financial resources have been reluctant to recognize the equality of Russian counterparts when defining objectives, designing project components, developing metrics of success, and jointly managing the overall relationship. Sharing of costs and continued evolution toward truly joint efforts from the earliest stages of planning are essential if joint efforts are to receive political and financial support over the long term.

2. Support, or at least acceptance, by all concerned government agencies in both countries is an important first step in launching a new public- or private-sector initiative or even renewing existing arrangements. A common problem has been the absence at the discussion tables of representatives of one or more important government agencies from the two countries who should have direct interests in the project. Often, it is essential that relevant agencies participate in discussions of significant implementation details as well as simply giving general approval for the general approach.

Aside from the special foreign policy roles of the Department of State and the Ministry of Foreign Affairs in advocating joint activities that they consider important, there may not be effective champions within the two governments for guiding proposed activities. International policy officials may be supportive of specific projects, but they rely on technical agencies to work out details. The dispersion of authority among technical agencies requires considerable coordination from the outset. Also, the involvement of private-sector companies and independent research groups may further highlight the importance of coordination.

3. International programs sponsored by institutions in third countries that have objectives similar to those reflected in U.S.-Russian bilateral efforts may compete for the time of interlocutors and important scientific leaders in either

the United States or Russia. At the outset, the commitments of key interlocutors and scientists should be clear to both sides. The commitments should, to the extent possible, include reciprocal travel to consult on progress of the programs. If appropriate, important organizations from other countries might be considered as additional participants in the planned activities.

4. Cooperation that builds on mutual strengths of the two countries and extends ongoing joint activities of their institutions is usually on a solid footing. However, initiation of bilateral activities in some subfields of biology wherein one country has relatively limited experience will require considerable patience, with full recognition of the differences in capabilities. The expectations as to mutual scientific benefits need to be carefully considered, depending on the comparability of capabilities and interests.

5. Strong commitments and support by institutions in both countries that are participating in bioengagement are essential. Such support includes releasing key participants from other duties when necessary; providing appropriate working facilities for participating scientists; ensuring access by research teams to water, power, communications, maintenance, and transportation infrastructures of the institutions; and arranging facilitative services for visiting scientists.

6. The importance of up-front planning, including pilot efforts if appropriate, prior to initiating significant program activities cannot be overemphasized. A get-acquainted phase that involves clarification of tasks, agreements on responsibilities and time lines, and preliminary identification of desired outcomes may be essential.

7. Development of strategies for achieving long-term support of important activities deserves high priority. Government agencies and other organizations operating on year-by-year budget allocations often have difficulties in considering the implications of long-term programs. But continuation over the long term is often a key to significant payoff from some programs.

In short, wide-ranging consultations on details of proposed projects and discussions of preliminary plans for extending successful efforts are highly desirable early steps. Metrics include, for example (a) follow-on activities such as success in applying for additional grants, (b) realization of plans for publications, (c) filing of patent applications that draw on collaborative research results, (d) improvements of facilities to overcome technical weaknesses in the laboratories that may emerge during initial cooperative activities, (e) adoption of new protocols or procedures that have demonstrated success, and (f) enrollment in the cooperative activities of talented young investigators who are interested in linking their early careers to international projects.

8. The two governments have expanded their initial visions of narrow nonproliferation approaches, recognizing that strengthening broadly based institutional infrastructures is a key aspect in addressing bioterrorism and proliferation concerns. Indeed, a capacity-building approach when considering biosecurity and biosafety is imperative.

Of special importance is recognition that even in narrowly defined security-oriented programs directed to prevention of bioterrorism, attention to common health and agricultural diseases that affect many people and agricultural resources may be essential. Broad recognition of health concerns, in particular, is usually as important for local acceptance of programs as narrowly focused concerns over the much lower probability of outbreaks of diseases associated with extremely dangerous pathogens. By including a strong emphasis on day-to-day issues facing the general public, local buy-in of programs will be significantly enhanced. Then cooperative activities can be better oriented to addressing key components of overall health, agriculture, and other systems that intersect with bioterrorism concerns.

9. The involvement of anticipated users of results of applied research activities early in the design and conduct of research projects is desirable. The users may be government agencies, specific facilities, industrial organizations, or clusters of professional organizations. Often, planning should extend well beyond expectations for preparation of journal articles and extend all the way to the marketplace, although journal articles may be an essential first step.

10. Selecting, installing, and maintaining new equipment, including imported items, may be a critical component of a joint project. However, the long-term costs of equipment acquisition and maintenance (including warranties), the skills needed to utilize the equipment effectively (including technicians), and the support infrastructure for supplies and services (relying on readily available local experts for maintenance of laboratory equipment) may vary significantly, even though the equipment is designed to serve comparable functions at different locations. All aspects of equipment acquisition, utilization, and maintenance need to be carefully considered when planning collaborative activities that require such acquisitions. Compliance with local quality assurance requirements for data that are generated and adherence to prescribed environmental practices in the laboratory and in the field deserve special attention.

LESSONS LEARNED BY RESEARCH SCIENTISTS

To obtain working-level perspectives as to lessons learned, the committee solicited reflections on personal experiences of a number of scientific collaborators in the two countries who had been active in one important area of bilateral cooperation—joint research in the field of agriculture. The collaborators provided their observations concerning the successes of their project activities, the reasons for success, problems encountered, and lessons learned for future projects. A number of their viewpoints are set forth below, and their observations are further elaborated in Appendix C.10. Their impressions underscore the importance of synchronizing solutions to problems encountered at the governmental and institution levels with solutions of problems encountered at the level of the researcher.

While the comments focused on improving cooperation in the area of agriculture, some observations have salience in other fields as well.

International projects may have been a new experience for some scientists, although this situation may be of less concern in the future as international outreach continues to expand. At times a resident of one country must relocate for a period of months or longer to the other country as a manager, as a highly trained specialist in a newly developing area of endeavor for the host country, or as a trainee. Lack of experience in working in foreign environments or unfamiliarity with the requirements of international projects can lead to many missteps—administratively, financially, or programmatically. Care should be taken in selection of the people who relocate or travel abroad, and reliable support mechanisms may be needed to avoid difficulties that reduce productivity or create personal hardships for temporary visitors.

While researchers sometimes have a sufficient degree of fluency in the language of their international counterparts to carry out general exchanges of views and minor transactions, interpreters are often essential in development and implementation of long-term arrangements. Special language training may be needed for scientists who will spend weeks or even months in a partner country. Also, written agreements between the U.S. and Russian institutions are usually considered to be significant documents and may require translations. Some plans fail to allocate sufficient budget resources to language training or professional interpretation services.

Other concerns of participating scientists are reflected in the following 12 observations.

1. Too often, interested parties assume that government approval of a collaborative project means that adequate financing will be provided by one or both of the governments until the project is completed. Often this is not the case. Even if a first round of funding is provided, a planned second round may again require an extensive list of approvals with no assurance of a positive outcome. Proponents in one country of a proposed project, whether financed by a public-sector or private-sector organization, need to take care in avoiding statements that lead to false expectations among their counterparts as to commitments of financial sponsors that will support projects.

2. Key collaborators for individual projects should have common interests and capabilities that are well matched. Cooperative projects should not be undertaken if the principal scientists in the two countries are not satisfied with the content of the proposed programs and the capabilities and enthusiasm of their counterparts. Compatibility issues can be addressed during an initial get-acquainted phase prior to launching the project.

Sometimes senior scientists with somewhat different interests and research objectives are designated to serve as the coleaders from the two sides of projects that had been developed by others. In these cases, the leaders have the options of (a) embracing previous arrangements, (b) attempting to redefine the programs with their counterparts, or (c) stepping down and arranging for other project leaders.

3. In-person joint planning and review throughout the implementation of projects is important. Time lines for carrying out different phases of research are a continuing topic, and preliminary agreement on publications and authorship as well as other anticipated outcomes of collaboration needs to be reached early in the project and adjusted as necessary. In short, face-to-face field and laboratory visits at predetermined intervals may be essential, not only to coordinate activities but also to clarify misconceptions about the research approach and to build mutual confidence of reliability of foreign partners.

4. Open communications that facilitate access to primary data, interim results, and modifications of research approaches are important throughout project implementation.

5. Joint activities are most interesting for both researchers and policy officials when they are results oriented. Publications, presentation of concepts and technical data to likely users of research findings, and, in some cases, patent applications are often cited as desired results. This orientation of international projects to providing discernable outcomes is particularly important in supporting requests for future funding, which may be in competition with requests for funding of domestic projects.

6. Arrangements for funding joint projects will, of course, depend on the type of funding that is available. If grants are obtained, payments to the participating institutions and scientists in the projects should be linked to completion of predefined tasks specified in the grants. This approach helps to ensure that grant funding is focused on the tasks at hand and not used for other purposes.

7. Special efforts may be needed to involve investigators who are in the early stages of their careers in joint projects when appropriate. They not only can help ensure long-term continuation of research efforts, they also can provide continuity of current efforts when more senior scientists are unexpectedly drawn to other projects or retire. But most important, they may be able to bring fresh ideas to projects that might otherwise be stymied by out-of-date concepts.

8. The more institutions that are involved in cooperative projects, the more important the agreed administrative arrangements become. One-on-one institutional arrangements may seem to work better and more efficiently than broader involvement of a number of institutions in a single project. At the same time, however, involvement of specialists from a number of institutions with particular skills and experiences may be important in building self-sustaining networks of specialists. In any event, when organizational affiliations of project participants expand, steps are needed to simplify administrative arrangements to the extent possible.

9. At times, newly constructed or reconstructed facilities are needed to

carry out joint projects. Allowances must be made for unanticipated difficulties and time delays that may accompany the initial uses of untested facilities.

10. There may be requirements for special facilities and procedures to accommodate new projects. For example, requirements by government funding agencies related to animal care and use may extend beyond previous requirements set forth by individual facilities, and adjustments are then clearly in order.

11. The presence in Russia of an organization that can assist investigators in resolving difficulties across borders that may arise during project implementation—in particular, the International Science and Technology Center (ISTC)—has been important. Now, as the ISTC prepares to close its doors in Moscow in 2015, there may be a need for another mechanism or mechanisms to help facilitate activities.

12. Professional rewards from collaboration can be high. Collaboration not only helps solve problems of direct interest to principal investigators, but also highly visible joint efforts can at times encourage other colleagues to become involved in international programs.

Many other lessons learned are included in scientific publications, trip reports, and other manuscripts prepared by scientists involved in exchanges during the past decade. The best way to take advantage of their experience is, of course, through direct contact with them. This report is intended to provide useful pointers for beneficial discussion.

As to future programmatic activities, some problems are likely to continue to complicate cooperation in science-oriented activities sponsored by the governments or by other organizations in the two countries. Hopefully, experiences in resolving past difficulties have sensitized the participating organizations in both countries to resolve anticipated issues as soon as possible after authorized counterparts have given “approval in principle” to move forward with projects. While impediments may continue to arise, early resolution will probably be quicker than resolution that is postponed to the implementation stage.

9

Strategies and Coordination

As we have seen, the life sciences encompass a wide variety of interests and activities. Cooperative programs are quite diversified. The organizations involved in developing and implementing joint efforts are numerous.

While preparation of a single unified strategy on overarching goals, objectives, and approaches for bioengagement that could be adopted by the two governments is unrealistic, oversight of important elements of bioengagement both at high governmental levels and at working levels has been important in the past. Now, supportive oversight by the two governments will be particularly significant as scientific leaders in the two countries consider adjusting their program priorities and budgets to correspond with changes in the political and economic environments, globally and bilaterally, that affect cooperation.

Broad statements by the governments concerning common interests have frequently provided general guidance on important program goals and activities. As underscored in previous chapters, in the life sciences there are many examples of program approaches that have led to scientific, environmental, social, economic, and security benefits for both countries. Official pronouncements concerning joint approaches have often been useful in focusing attention on successes and on future opportunities for cooperation that build on past achievements.

JOINT PROGRAM STRATEGIES

At times, the U.S. and Russian governments—and also private-sector institutions in the two countries—have adopted broad program strategies for helping to guide clusters of bilateral activities in areas of particular interest. Occasionally, these strategies have been jointly developed and incorporated into agreements (e.g., agreement between the National Institutes of Health and the Russian Academy of Sciences in 2011, which involves additional institutions from both sides as well). More frequently, each side has developed its own program strategy, taking into account—at least to some extent—the priority interests of the other side. In both countries, organizations interested in bioengagement must often present to budget officials the political, economic, and scientific contexts for requests for funding of relevant activities.

Intergovernmental agreements sometimes set forth important frameworks for programs. More detailed approaches have been included in (a) memoranda of understanding involving government departments, ministries, or institutions in the two countries (e.g., many memoranda and protocols concerning health cooperation); (b) government calls for proposals from the scientific community for cooperative projects, which are to be submitted by interested organizations in parallel in each country (e.g., parallel calls during 2007–2009 for proposals for collaborative high-technology research at universities in the two countries by the Department of Education and the Ministry for Education and Science); or (c) jointly developed program documents that provide the frameworks for specific bilateral activities (e.g., project agreements based on the International Science and Technology Center [ISTC] model agreement of 1998).

At times, agreements provide "umbrella" provisions for activities in a variety of fields, with the biological sciences only one of many fields of interest (e.g., Agreement on Science and Technology Cooperation renewed in 2010). A few agreements have been focused specifically on selected aspects of the biological sciences (e.g., Protocol of Intent between the Centers for Disease Control and Prevention and Rospotrebnadzor of 2012, which was directed to reducing communicable and noncommunicable diseases).

In addition, general approaches to bilateral scientific cooperation are frequently discussed during formal meetings and informal consultations between representatives of the concerned organizations—such as ministries or universities—of the two countries. The results of these discussions are then reflected in subsequent actions by the parties to the discussions. The details may or may not be set forth in agreed documents.

Many private companies, universities, and nongovernmental organizations have their own strategies that they have developed with counterparts in the other country (e.g., contract of 2012 between the Skolkovo Foundation and the Massachusetts Institute of Technology on establishment of the Skolkovo Institute of Technology). At times, the approaches have been explicitly endorsed by the two governments, often reflecting financial and other types of support to be provided by the governments for the activities (e.g., announcement in 2012 by the two governments of joint efforts to help eradicate polio in Uzbekistan). At other times, the governments have applauded planned cooperative activities, even though they have not been directly involved in the development of the agreed approaches.

Frequently, individual institutions, and particularly private companies and universities, have used their own internal resources to develop and begin implementation of cooperative activities that are of interest to them and their foreign counterparts (e.g., training programs organized in 2009 by Purdue University, with support of Eli Lilly and Company, to train Russian specialists in the conduct of clinical trials). Occasionally, these initial contacts develop into larger efforts supported by the two governments or by private funding. Others have remained quite focused and limited in scope.

Whatever form formal arrangements take, persistence to continue cooperation over many years within an agreed framework of understanding has often contributed both to the advancement of science and to the strengthening of bilateral relationships. But at the same time, some institutional initiatives have been short-lived due to (a) financial, administrative, or technical difficulties that were not foreseen or adequately considered when the contacts were first developed or (b) erosion of interest of the early advocates of cooperation.

Agreements setting forth long-term strategic approaches (e.g., more than 5 years) have been few in number. Still, an agreement of indefinite duration may become a long-term arrangement (e.g., agreement between the Fish and Wildlife Service and the Ministry for Natural Resources that dates from the 1990s). Long-term commitments that are set forth in formal arrangements, such as those included in the 10-year intergovernmental Agreement on Science and Technology Cooperation (once renewed in 2010), are almost always cast in very general terms. Thus, they are more useful in providing a basis for international activities that is respected in both countries than in proscribing the specific types of activities that are to be pursued. Most agreements contain commitments for periodic consultations to review progress in implementing agreed activities and to consider future activities (e.g., Agreement on Cooperation in Science, Engineering, and Medicine between the U.S. National Academies and the Russian Academy of Sciences of 2008).

In the past, concerns about the inadequacy of financial resources for bioengagement have often outweighed other issues that need to be resolved before the signing of agreements. Frequently, agreements have been signed without assurance that funds will be available for implementation. As budgets become tighter, concerns over false expectations as to program activities increase.

In summary, joint program strategies are important, although they may take many forms. Typically, they are carefully developed on a joint basis. And the participating institutions usually make a commitment to implement a joint strategy, at least at the outset. It may be necessary to adjust strategies as projects are formulated and implemented. Such adjustments should, of course, involve the support of all participating parties. The need for a strategic approach to biodiversity, for example, is set forth in Box 9-1.

Box 9-1
Preservation of Biodiversity of the Northern Hemisphere

Russia and the United States are home to a significant portion of global biodiversity, including northern coniferous forests of the taiga, tundra, and other ecological zones. As human activities intensify and climate changes, preservation of these economically and environmentally important species is increasingly difficult. The enormous ecosystem services that they provide are poorly understood, and opportunities abound for Russia and the United States to jointly improve understanding of these services for the common good.

SOURCE: Leading American biodiversity expert, August 2012.

THE BILATERAL PRESIDENTIAL COMMISSION

As noted in earlier chapters, in 2009 the two governments established a Bilateral Presidential Commission (BPC). The BPC established a wide-ranging framework for intergovernmental cooperation in many fields, setting forth some principles that are akin to pronouncements found in very broad strategy documents. (See Appendix E.1.)

Twenty-two working groups were active in September 2012 under the umbrella of the commission. At least six considered activities involving the life sciences. At times, the efforts supported by one of the working groups have overlapped with interests of other working groups, but this has not become a major concern. The six working groups are as follows:

1. Health
2. Agriculture
3. Environment
4. Education, Culture, Sports, and Media
5. Science and Technology
6. Innovation

In general, the working groups have concentrated on providing political support for programs with near-term program payoffs of mutual interest. Special attention has been given to reducing impediments to implementation of programs. Probably their most important contribution has been the forums they have provided for senior policy officials to focus on engagement.

The lack of funding for carrying out innovative ideas has been a frequent concern of members of the working groups. In principle, a working group may bring to the attention of the leadership of the BPC opportunities for a new high-payoff initiative. The BPC may then encourage appropriate organizations in each country with access to funding for the initiative. However, they have been quite focused on near-term actions, which already have commitments of funding that will quickly lead to results of interest to the two governments.

Given the broad-ranging bioengagement activities that cross a number of working groups, the BPC could usefully organize overarching reviews of bioengagement activities, perhaps biannually. These reviews could include activities of the private sector as well as government-sponsored activities. In view of the rapid advancement and spread of biotechnology capabilities throughout the world and the impacts of such advances on the very essence of life (e.g., health, food, and environmental conditions), the reviews could be important not only in improving coordination and stimulating joint activities but also in bringing to the attention of interested scientific communities approaches that have proven valuable.

ROLE OF THE ISTC AND FUTURE COORDINATION

For the past 18 years, the International Science and Technology Center has provided a useful mechanism for facilitating development and implementation of many bilateral as well as multilateral projects in the life sciences carried out in Russia. The programs have been oriented in large measure to redirection to civilian tasks of underemployed former defense scientists. ISTC programs have also attracted participation of many other scientists who were not involved in defense activities, but who have high-technology skills. Past cooperative projects have often involved strong research institutions in the United States and Russia, while addressing pressing problems of the present and future.

The committee commends the achievements of the ISTC in facilitating hundreds of bioengagement activities. (See Appendix E.2.) Now, as Russia prepares to withdraw from the ISTC in 2015, the governments of the United States and Russia, along with other ISTC parties, need to carefully consider how they can continue to benefit from the positive legacies of the center in promoting successful international engagement in the life sciences. There has been much discussion in Moscow and in other capitals as to whether a successor organization to the ISTC that emphasizes international science cooperation, and only secondarily promotes nonproliferation objectives, should be established in Moscow.

For many years, Russia has been a principal beneficiary of programs facilitated by the ISTC. Russia now has a responsibility to help ensure that the details of the unique and highly successful experiments of the ISTC in the biological sciences, as well as in other fields, will continue to be available to the international community for the indefinite future. The United States and other ISTC parties can assist in this effort, but Russia has important perspectives and insights that are essential in capitalizing on 18 years of international investments in ISTC activities.

As the ISTC experiment comes to an end in Russia, a new phase of cooperation should be developed and become even more successful. The current trend is to emphasize cooperation in rapid development of biotechnology capabilities of interest to organizations in both countries. But such an effort can only be successful if buttressed by strong basic research capabilities in the two countries, as discussed in Chapter 10.

In principle, bilateral cooperation organized by individual scientists on their own is certainly possible and highly desirable. In the ideal case, these scientists should need to rely only on their partners in the other country for facilitative services, e.g., arrangement of visas, travel, working areas, and so on. Of course, the interested U.S. and Russian partners must have the necessary financial resources and must be prepared to work within the confines of export control and other international agreements and national laws that define constraints on cooperation.

Three observations are offered concerning the facilitating of cooperative research activities, following the closing of the ISTC office in Moscow. The need for different types of arrangements will depend on the extent to which the U.S. and Russian governments, and to a lesser extent nongovernmental entities, finance cooperative activities.

1. The two governments have science-oriented diplomats at the U.S. Embassy in Moscow and the Russian Embassy in Washington, and they can at times help facilitate cooperative science activities.
2. In Chapter 10, a recommendation of the committee to establish a new bilateral Research Fund is presented. The fund should take on responsibility for supporting implementation of the grants that it awards—a modest but still important task.
3. The working group on impediments of the Science and Technology Working Group of the BPC will presumably continue to improve implementation procedures of the two countries and could give special attention to adjusting to the aftermath of the ISTC.

10

Recommendations for Future Bioengagement

The Introduction of this report underscores the difficulty in estimating direct and indirect costs of public and private investments in bioengagement activities. While estimates are far from precise, they clearly indicate that annual investments of the two countries in bioengagement decreased from more than $100 million a decade ago to less than $25 million in 2011. Many important bioengagement collaborations have terminated, and significant opportunities for pursuing innovative joint efforts have been lost. This chapter recommends appropriate investments that will revitalize bioengagement while advancing broad-ranging interests of both countries.

Some bilateral programs described in Chapters 2, 3, 4, and 5 and in the appendixes will probably continue to receive financial support by the two governments and by the private sector, without the need for new advocacy efforts (e.g., cooperation in surveillance and reporting of infectious diseases that cross international borders, and responses to market demands for express diagnostic tools). However, many other programs based on important mutual interests in bioengagement will be terminated or may not even begin if governmental funding for bilateral activities continues to decrease.

The overall level of bioengagement activities is determined by many individual decisions of a wide variety of funding and implementing organizations in the two countries. Each organization has its own priorities and financial constraints, and the criteria in selecting projects for support vary across funding organizations. Projects advocated by different organizations simply do not compete one-against-another in practice.

Thus, the committee is not in a position to select specific programs that deserve priority in competition with other bilateral or international programs.

However, the committee has identified promising areas of research for consideration by governments and the private sector as priorities for collaboration. Then action-oriented political decisions, supported with financial commitments, at senior levels of the two governments are needed to implement recommended approaches, if the uniqueness of the U.S.-Russian relationship in the life sciences is to be maintained.

THREE RECOMMENDATIONS

Given the benefits from U.S.-Russian bioengagement activities that have been repeatedly recorded in recent years, **the committee recommends continuation and, to the extent possible, expansion of U.S.-Russian programs** that have been considered by the sponsors and the participants in the two countries to have been successes and hold promise for even more fruitful rewards in the future. Much of the focus will probably be on themes wherein Russian strengths are recognized internationally as complementing capabilities of the United States, which is the global leader in many fields.

The current portfolio of current bioengagement projects includes only a few activities directed primarily to nonproliferation or science-infrastructure enhancement in Russia, the main emphasis when bioengagement was on the rise in the early 2000s. The several activities that are currently directed to these objectives are devoted in large measure to transferring U.S. experience to Russian institutions that are rapidly accepting the responsibility and financial burden for their own activities. At the same time, however, there is increased appreciation in both countries of the importance of strengthening public health and agriculture production systems on a broad basis for not only achieving health and food goals but also contributing to achievement of security and environmental objectives. Most projects that are currently in place are intended to meet goals of the future without clinging to outdated objectives of the past. Such forward-looking projects deserve special attention as the overall character of the U.S.-Russian relationship continues to evolve.

Second, **the committee recommends establishment of a bilateral research fund** to enable highly qualified specialists in the two countries to join together in new collaborative endeavors at the leading edge of the life sciences. The emphasis is on strengthening basic research, which is essential in providing the ideas and skills for eventually taking scientific achievements to the public- and private-sector markets. In each country, strong research capabilities should undergird development of biotechnology efforts that are internationally competitive and in time should become self-supporting. Many highly qualified research institutions in the two countries have demonstrated their capabilities to be stable and reliable focal points for productive bioengagement. The new fund, which would build on these capabilities, is discussed later in this chapter. Illustrative research areas that are particularly attractive for collaboration are identified.

Third, earlier chapters have identified both (a) steps that can facilitate implementation of joint programs and (b) difficulties that continue to inhibit effective collaboration. Thus, **the committee recommends that the two governments continue their efforts to reduce the impediments to cooperation.**

In previous chapters, the problems associated with visas, taxes, customs, intellectual property rights, export control, financial accountability, lack of transparency, and other common difficulties were discussed. The time and resources lost in coping with administrative issues should be minimized. The Science and Technology Working Group of the Bilateral Presidential Commission should continue to focus on improving policies of the two countries that reduce administrative complications of joint scientific efforts.

ELABORATION OF PROPOSAL FOR A NEW BILATERAL RESEARCH FUND

The committee recommends that the two governments establish the new research fund under the direction of an independent board of directors, with its members appointed by the two governments (e.g., perhaps five established scientists from each country who would be ineligible to compete for project awards by virtue of their membership on the board). The fund should have small offices in both countries, hosted by respected scientific organizations in the countries that have existing authorities to award research grants, thereby eliminating the need to establish new legal entities, at least at the outset of activities. The fund should encourage American and Russian scientists from interested research institutions to jointly design projects that enhance important components of the research and development cycle, with special emphasis on basic research activities of national and global importance. (Appendix F.4 identifies other international efforts to provide funding mechanisms that were considered.)

The committee is not in a position to determine the most appropriate host organizations in Russia or the United States where the offices of the fund would be embedded. The two governments must weigh a number of organizational and financial issues in making such determinations. Also of importance will be the views of the scientists and others who are selected to lead the fund.

The emphasis on basic research is important, given the current trends in Russia to invest an excessively large proportion of available resources for life science initiatives into applied research and development activities with the possibility of near-term payoffs (e.g., policies of Rusnano). Thus, the significance of the proposed fund as a complement to other unfolding opportunities that stress biotechnology is clear. In the long run, the basic research component of activities in both countries will be essential in advancing biotechnology.

Each project supported by the new fund should be of scientific interest to researchers in both countries. To attract leading scientists and to help build lasting networks of scientists with common interests, most projects—selected on the basis of carefully structured peer reviews—should be relatively large (e.g., up to $2 million for 3-year projects). At times, clusters of small projects focused on related objectives might be bundled as a single project. Each side should commit to equal funding; and they should then disburse their financial resources in a coordinated manner, with about 50 percent of the overall funds directed to collaborating institutions in each country. The division of funding responsibilities for individual projects will undoubtedly vary.

The fund should have a project development component. Scientists, and particularly young investigators, who have good ideas but not strong existing connections with colleagues in the other country might be awarded small travel grants on a competitive basis. They would then have an opportunity to interact with potential partners and, if appropriate, develop with colleagues proposals for consideration by the fund. This get-acquainted approach has been quite useful in the development of linkages in the past.

Among the criteria that should be considered in selecting recipients of research awards are the following:

- Uniqueness of the combined capabilities of the Russian and U.S. scientists to address technical issues that are important in achieving both national and global scientific objectives.
- Involvement of scientists in international cooperation during the early stages of their careers, thereby increasing the likelihood that successful cooperation will be continued for a lengthy period.
- Contribution of the research in demonstrating how a culture of responsible science should pervade many global research activities, with particular attention to conservation of biological resources and to mitigation of concerns over inappropriate use of sensitive technologies.

Given the breadth of the life sciences, the annual launch of 15–20 projects over a period of 5 years would engage a number of key laboratories and specialists in a number of important and rapidly developing scientific relationships. Highly visible and easily understood outcomes would be the goal for each project. Successful efforts would in some cases attract additional follow-on support from other national and international sources. Such sources would include, for example, the previously identified new outreach initiatives being developed by the Russian government, such as the Skolkovo initiative, and currently latent interests of the U.S. private sector in research and manufacturing investments in Russia.

Among the topics that could be considered for joint investigations are the following:

- Novel therapeutics, diagnostics, and vaccines. Examples are multidrug-resistant tuberculosis therapies, rapid and inexpensive point-of-care diagnostics for both common and rare but devastating diseases, inexpensive and reliable water and food quality testing, viral therapeutics, and stem cell therapies.

- New preparations and drugs for combating cancer, together with new methods for diagnosis and treatment of cancer.
- Improvements in disease surveillance and monitoring techniques of priority interest to the two countries. Examples are molecular and genetic studies of influenza, viral infections linked to oncology diseases, respiratory infections, intestinal illnesses, and vector-borne diseases.
- New approaches and techniques in synthetic biology. Examples are investigations of genome, proteome, and metabolic pathways; development of improved diagnostic tools; and studies of chemical and protein synthesis.
- Animal health and latent zoonotic diseases. Examples are avian influenza, porcine reproductive and respiratory syndrome, African swine fever, and foot-and-mouth disease.
- Plant resilience. Examples are control of potato blight and soybean and wheat diseases; adapted cultivars for alfalfa and grapes; protection against invasive weeds; and genetic modifications to reduce disease susceptibility.
- Understanding and preservation of biodiversity. Examples are cataloging and analyzing plant, animal, and microbial biodiversity in contaminated and pristine ecological regions, including regions distant from large urban centers.
- Research with highly dangerous pathogens requiring specialized biocontainment facilities and highly experienced staff capabilities. Examples are investigations of Ebola, Marburg, and variola viruses of special interest to the governments.
- Development of medical software. Examples are improved telemedicine methodologies, and upgrading of medical database technology and transfer.
- Investigations of antidotes to counter adverse health and ecological aspects of organophosphorous compounds used in pesticides and herbicides.

Each award could involve not only two lead laboratories but other supporting laboratories on each side as well, thereby building expanded networks of collaborators that would strengthen the future international framework for collaboration. As previously noted, these networks might also include clusters of small groups of researchers from different institutions.

An early concern of the committee was the capabilities of a sufficient number of Russian laboratories to operate at the international level for such a program. However, the Russian Academy of Sciences has several hundred biological research laboratories that have capabilities of worldwide interest. Expanding this estimate to include laboratories of all three Russian academies, Russian universities, and branch institutes in Russia, there are a sufficient number of well-rated Russian laboratories to warrant establishment of the program—with 5 to 20 experienced investigators and highly talented young investigators in each laboratory.

As to the size of the grants, the megagrant program of the Russian government provides 3-year grants of $5 million to individual universities that are expected to create new research laboratories with outreach internally and internationally. At the other extreme, the Russian Foundation for Basic Research provides small grants, usually less than $25,000 to support individual investigators within Russia. As yet another relevant example, a World Bank program in Kazakhstan provides 3-year grants of $1.5 million to laboratories that intend to pursue research that leads to commercialization of research results. In the United States, the size of grants varies greatly depending on the purpose of the grant and policy of the funder. Grants to establish centers of excellence sometimes provide several million dollars per year, with the grants renewable after an initial 5-year award period. Thus, the proposed size of the new grants seems to be reasonable. In building networks of universities, larger projects (including subprojects) are most likely to have lasting impacts.

Once the topics of mutual interest are determined, a scenario such as the following could be followed, although the governments might well decide to modify the approach as they work out the details.

- The board of directors would issue unified calls for research proposals to be prepared jointly by teams of scientists from the two countries. These calls would reflect agreement within the board on research priorities, anticipated outcomes, and range of funding levels. Lessons learned set forth in this report might also be important in shaping the approach.
- The board would refer proposals that are received to appropriate peer reviewers in the two countries. The board members would then meet to consider jointly the results of the peer review and to select the winners of each competition. Competitions might be held on an annual basis.
- The Russian financial contributions to the program would be used to cover the costs incurred by Russian participants in projects, and the U.S. contributions would cover the costs incurred by the American participants. Usually, there would be no need for cross-border transfers of funds. The division of funding need not be equal for each project, but in the aggregate there should be an equal sharing of the costs.
- The board's staff would arrange for periodic reviews and evaluations of the funded projects, and it would assist award recipients in making arrangements for carrying out projects.

MOVING FORWARD

In summary, an overall bioengagement effort that adequately reflects the importance of bilateral collaboration can be achieved by a combination of (a) increased support for carefully selected ongoing cooperative programs, and for currently dormant collaborations that have proven their value in the past, (b) a new bilateral research fund that supports joint research projects selected on a competitive basis, and (c) an increased emphasis on reducing impediments to carrying out approved projects. Both governments should take the initiative for and share the costs of these recommendations.

Clearly, with additional financial support on both sides there could be new productive joint efforts to (a) capitalize on the capabilities of revitalized world-class scientific institutions of Russia that are ready to deepen cooperation with American colleagues, (b) lead global efforts in addressing selected global and regional issues requiring new and improved scientific insights, and (c) stimulate a global culture of "responsible biological science" that draws on U.S.-Russian experience in dealing with pathogens of concern and related technologies.

In looking to the future, of particular importance are the involvement of young researchers in bioengagement, a commitment of program managers to responsible science, incentives to offset the brain drain, and reporting of research results to the broader international scientific community in a timely and easily accessible way. These are keystones for long-term continuation of joint efforts.

Finally, the Russian government is in the process of terminating its involvement in the U.S.-sponsored Cooperative Threat Reduction Program administered by the Department of Defense (the Nunn-Lugar Program), foreign assistance efforts of the U.S. Agency for International Development, and activities of the International Science and Technology Center. These three programs have been important pillars of U.S.-Russian bioengagement efforts for many years. Also, as we have seen, during the past several years, the U.S. government has significantly reduced financial support for bioengagement through these and other channels in favor of other budgetary imperatives.

Despite the foregoing developments, the committee responsible for this report considers that the case is strong for expanding U.S.-Russian bioengagement, even in the face of budget stringency by both governments. The stakes are significant, the established base for collaboration is unprecedented, and many of the potential payoffs are clear. The broad-ranging assessment in this report of lessons learned and of future collaborative opportunities should help ensure that the governments and the scientific leaders in both countries now give adequate attention to the many dimensions and rewards from bioengagement.

Rewards are often measured in terms of research discoveries, development of new products, improved health and agriculture services, and protection from misuse of biotechnologies. While these indicators of success are important, the major payoff from new-found friendships across the ocean, an outcome that can last for decades, is the network of scientists who are interested in working together—through visits, conference attendance, e-mails or other means—during many years of their professional careers. There is no better assurance than the respect and camaraderie surrounding such friendships that the life sciences will indeed be used for the betterment of the global population.

Appendix A

Available Resources

Appendix A.1

Biographical Sketches of Committee Members

Peter H. Raven (*committee Co-Chair*) is a member of the National Academy of Sciences. He is president emeritus of the Missouri Botanical Garden, after serving as president for three decades, and is recognized as one of the world's leading botanists and advocates for conservation and biodiversity. He received the National Medal of Science in December 2000. He has also received numerous other awards, including the Society for Conservation Biology Distinguished Service Award, International Prize for Biology from the government of Japan, Environmental Prize of the Institute de la Vie, Volvo Environment Prize, Tyler Prize for Environmental Achievement, and Sasakawa Environment Prize. He is Engleman Professor of Botany at Washington University and chairman of the National Geographic Society's Committee for Research and Exploration. He has served as president of the American Association for the Advancement of Science and as a member of the President's Committee of Advisors on Science and Technology. He served for 12 years as home secretary of the National Academy of Sciences. He is a member of academies of science in Argentina, China, India, Italy, and Russia. He was first chair of the U.S. Civilian Research and Development Foundation. He has received honorary degrees from universities throughout the world.

Valentin Vlassov (*committee Co-Chair*) is a member of the Russian Academy of Sciences (RAS) and vice chairman of the Siberian Branch of the Russian Academy of Sciences since 2008. He also currently serves as the director of the Institute of Chemical Biology and Fundamental Medicine of the Siberian Branch of RAS and as professor of molecular biology and chair of the Department of Molecular Biology at Novosibirsk State University. He also is chair of the Biological Council of the Siberian Branch of RAS, which coordinates research at biological academic institutes in Siberia. He has more than 300 scientific publications that include research on RNA structure, antisense technologies, and circulating nucleic acids. He has received several awards, including the State Prize for scientific achievement. Current activity is focused on development of approaches for translational medicine, including postgenomic technologies-based diagnostic methods, design of gene-targeted therapeutics, and cell technologies.

Kavita M. Berger is the associate program director of the Center for Science, Technology, and Security Policy at the American Association for the Advancement of Science (AAAS). Since joining AAAS in 2006, she has addressed complex biosecurity policy issues, such as personnel reliability and misuse of biological research, by actively interacting with the scientific community, facilitating open dialogue between the scientific and security communities, and providing a voice for the scientific community in timely policy debates. Through these projects and other activities, she has helped enable scientists to contribute to addressing biosecurity risks at the local, national, and international levels. During a short absence from AAAS, she worked with the Presidential Commission for the Study of Bioethical Issues as the staff lead on evaluation of the ethical issues associated with pediatric medical countermeasures research. She received her Ph.D. degree in genetics and molecular biology at Emory University and conducted her postdoctoral research on preclinical research and development on HIV and smallpox vaccines.

David Franz (*Consultant*) has recently served as vice president and chief biological scientist of MRIGlobal and senior advisor (biosecurity engagement) to the Office of the Assistant to the Secretary of Defense for Nuclear, Chemical, and Biological Defense Programs. Dr. Franz was the chief inspector on three UN Special Commission biological warfare missions to Iraq and served as technical advisor on long-term monitoring. He also served as a member of the first two U.S.-U.K. teams that visited Russia in support of the Trilateral Joint Statement on Biological Weapons and as a member of the Trilateral Experts' Committee for biological weapons negotiations. Dr. Franz served in the U.S. Army Medical Research and Materiel Command for 23 of 27 years on active duty and retired as colonel. He served as commander of the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) and as deputy commander of the Medical Research and Materiel Command. Prior to joining the Command, he served as group veterinarian for the 10th Special Forces Group (Airborne). The current focus of his activities relates to the role of international engagement in the life sciences as a component of national security policy. Dr. Franz holds a D.V.M. from Kansas State University and a Ph.D. in physiology from Baylor College of Medicine.

Tatiana Gremyakova is chief science coordinator of biotechnology at the International Science and Technology Center (ISTC) in Moscow. She graduated from the Medical-Biological Faculty of Moscow Medical Institute (1979) and received her Ph.D. degree at the Moscow Mechnikov Institute of Vaccine and Sera (1983). She joined the State Research Center for Applied Microbiology in Obolensk, and received her doctor of medical sciences degree in 2004. Her areas of interest are microbiology, biochemistry, diagnostics, drug and vaccine development, biosafety, and biosecurity. She is the author of nearly 70 Russian and international scientific publications. She has served as chair of the ISTC's BioCom, where she developed and managed projects with governmental and business partners. She has participated in developing more than 150 international projects (R&D and science infrastructure) in medicine, pharmacology, agriculture, industrial biotech, biosafety, and physical security in Russia, Armenia, Belarus, Georgia, and Kazakhstan. Currently, she serves as an expert at the Analytical Center of the Russian Government, where she supports projects of interest to the President's Commission on Modernization and Technological Development. She is a member of the International Society of Infectious Diseases.

Oleg Kiselev is a member of the Russian Academy of Medical Sciences. He is director of the Research Institute of Influenza in St. Petersburg. Currently a professor of molecular virology, he graduated from the internal medicine faculty of the I.P. Pavlov First Medical Institute. In 1972, he received his Ph.D. degree in biochemical genetics at this Institute in mitochondrial biogenesis, and in 1979, he received a doctor of science degree in molecular biology. Later, he moved to the Ministry of Microbiological Industry as head of the Division of Genetic Engineering for development and manufacture of recombinant interferon. He received patents for IL-2 and IFN-alpha producer strains and technology for their production. Beginning in 1988, he has served as director of the Research Institute of Influenza. The institute has become the national World Health Organization (WHO) Center for Influenza Control and Surveillance. The institute includes a Clinical Department headed by Professor Kiselev, where every year new influenza vaccines are tested and approved according to WHO recommendations. He has been the project leader on a number of international grants: DelNS–vaccine development and production (Green Hills Biotechnology); Antiinfluenza siRNA (SirnaOmics); new antiviral drugs and production technology—Triazavirin—with wide spectra of antiviral activity; and others in the field of influenza. He has published 12 books in the fields of influenza, prions, herpes virus infection treatment, papilloma virus pathogenesis, and cancer development.

James LeDuc is director of the Galveston National Laboratory (GNL) located on the campus of the University of Texas Medical Branch in Galveston, Texas. He is also a professor in the Department of Microbiology and Immunology and holds the Robert E. Shope and John S. Dunn Distinguished Chair in Global Health. He relocated to Galveston in 2006 from the Centers for Disease Control and Prevention (CDC), where he was the influenza coordinator. He also served as director, Division of Viral and Rickettsial Diseases, coordinating research activities, prevention initiatives, and outbreak investigations for viral and rickettsial pathogens, including viral hemorrhagic fevers, influenza and other respiratory infections, childhood viral diseases, and newly emerging diseases such as SARS. He served as the associate director for global health in the Office of the Director, National Center for Infectious Diseases at CDC, and he was a medical officer in charge of arboviruses and viral hemorrhagic fevers at the World Health Organization in Geneva, Switzerland (1992–1996). He also held leadership positions during a 23-year career as a U.S. Army officer in the medical research and development command, with assignments in Brazil, in Panama, and at various locations in the United States, including the Walter Reed Army Institute of Research and the U.S. Army Medical Research Institute of Infectious Diseases. He has published more than 200 scientific articles and book chapters.

Sergey Netesov is a corresponding member of the Russian Academy of Sciences. He has been vice rector (research) at Novosibirsk State University since 2007. Previously, he served for 30 years at the State Research Center of Virology and Biotechnology, Vector; and in 1990, he became its deputy director for research. He graduated from Novosibirsk State University (1975), joined Vector (1977), and received his Ph.D. (1983) and doctor of biology (1993) degrees. He is a member of the European Academy of Sciences, American Society for Virology, American and European Biosafety Associations, and the Russian Society of Epidemiologists, Microbiologists, and Parasitologists; he is also a member of the Filovirus Study Group of ICTV. In the beginning of his research career he developed original methods of isolation of restriction endonucleases and reverse transcriptase. Later, he was a principal investigator (PI) of a few national projects of pioneer sequencing the genomes of the following viruses: Marburg, Ebola, Venezuelan Equine Encephalitis (VEEV), Eastern and Western Equine encephalitis, tick-borne encephalitis, and influenza. He also was a PI of the reverse genetics project on the VEE virus reconstruction from cDNA fragments. He also was involved in the development of an inactivated hepatitis A vaccine and recombinant hepatitis B vaccine and ran a project on the development of a recombinant vaccine against VEE virus. Recently, he successfully completed a few projects focused on the study of molecular diversity and epidemiology of viral hepatitis in Siberia and participated in other molecular epidemiology projects. Dr. Netesov is twice a winner of the prize awarded by the government of the Russian Federation in the area of science and technology (1998 and 2006). His research interests include virology, biotechnology, and biosafety. He is the author of more than 140 publications in Russian and international journals.

Peter Palese is a member of the National Academy of Sciences. He is professor of microbiology and chair of the Department of Microbiology at the Mount Sinai School of Medicine. His research is in the area of RNA-containing viruses with a special emphasis on influenza viruses. Specifically, he established the first genetic maps for influenza A, B, and C viruses, identified the function of several viral genes, and defined the mechanism of neuraminidase inhibitors (which are now FDA-approved antivirals). He was also a pioneer in the field of reverse genetics for negative strand RNA viruses, which allows the introduction of site-specific mutations into the genomes of these viruses. This technique is crucial for the study of the structure and function relationships of viral genes, for investigation of viral pathogenicity, and for development and manufacture of novel vaccines. In addition, an improvement of the technique has been effectively used by him and his colleagues to reconstruct and study the pathogenicity of the highly virulent, but extinct, 1918 pandemic influenza virus. His recent work in collaboration with Garcia-Sastre has revealed that most negative strand RNA viruses possess proteins with interferon antagonist activity, enabling them to counteract the antiviral response of the infected host. At present, he serves on the editorial board for the Proceedings of the National Academy of Sciences. Dr. Palese was president of the Harvey Society in 2004, president of the American Society for Virology in 2005, a recipient of the Robert Koch Prize in 2006, and a recipient of the European Virology Award (EVA) in 2010.

Richard Witter is a member of the National Academy of Sciences. He served as a veterinary medical officer with the U.S. Department of Agriculture-Agricultural Research Service (ARS) Avian Disease and Oncology Laboratory (ADOL) in East Lansing, Michigan, for 38 years (1964–2002). He currently serves as collaborator with the ADOL and as adjunct professor with the Department of Pathobiology and Clinical Investigations at Michigan State University. He helped develop the first successful vaccine in the United States against Marek's disease and has documented the evolution of this virus to greater virulence. He has received numerous awards and recognition for his research. For more than 22 years, as director and research leader of ADOL, he administered a multidisciplinary research program on the biology of important avian viral neoplasms, as well as programs on recombinant DNA vaccines, immunogenetics, transgenic chickens, and genome mapping. He returned to the bench in 1998, where he pursued research on Marek's disease and avian leukosis until his retirement in 2002. He has been active in international activities involving grants programs in the Middle East and Central Asia. He helped initiate the ARS-Former Soviet Union Scientific Cooperation Program and has served as a scientific consultant to this program since its inception. He received his B.S. and D.V.M. from Michigan State University and his M.S. and Ph.D. from Cornell University.

Russ Zajtchuk, a national expert in telemedicine, is currently president of Chicago Hospitals International. For more than 27 years, he served in various positions in the U.S. Army, most recently as commanding general of the Army Medical Research and Material Command at Fort Detrick, Maryland, where he led development of a sophisticated telecommunications infrastructure to speed diagnostics, lab analyses, and consulting expertise worldwide. He is a cardiovascular surgeon who was professor and chairman of the division of cardiothoracic surgery at the Uniformed Services University of the Health Sciences. He also served as assistant surgeon general for research and development for the Department of the Army and as chief operating officer for the Department of Defense telemedicine test bed. He has served on several committees of the National Research Council concerning scientific developments in the former Soviet Union.

Sergey Zavriev is a corresponding member of the Russian Academy of Agricultural Sciences. He is head of the Molecular Diagnostics Department and head of the International Scientific Relation Department at the Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry of the Russian Academy of Sciences. His research during the past 10 years has been aimed at investigating plant virus genome structure and expression; cloning and expression of virus-specific genes, allergens and other proteins, and their application for functional studies; producing antibodies against different recombinant antigens, including allergens; development of technologies for PCR and RT-PCR-based detection of DNA- and RNA-containing pathogens; immuno-PCR technologies; and diagnostic kit production. He was previously a visiting professor in the Department of Plant Pathology at the University of North Carolina, where he worked on plant molecular virology. He has been awarded several international grants from INCO-Copernicus, INTAS, and European Commission FP6-FP7. He is a member of several international teams participating in the meetings and symposia on strategic studies of bioterrorism and biosecurity problems. He is the author of more than 140 articles, book chapters, and patents.

Appendix A.2

Relevant Reports of National Academies, Books, and Other Publications

NATIONAL RESEARCH COUNCIL (NRC), NATIONAL ACADEMY OF SCIENCES (NAS), AND INSTITUTE OF MEDICINE (IOM) REPORTS

- *What You Need to Know About Infectious Disease,* IOM, 2011.
- *Russian Views on Countering Terrorism During Eight Years of Dialogue: Extracts from Proceedings of Four U.S.-Russian Workshops*, NRC, 2009.
- *Global Security Engagement: A New Model for Cooperative Threat Reduction*, NAS, 2009.
- *The Biological Threat Reduction Program of the Department of Defense: From Foreign Assistance to Sustainable Partnerships*, NRC, 2007.
- *Biological Science and Biotechnology in Russia: Controlling Diseases and Enhancing Security*, NRC, 2006.
- *Innovating for Profit in Russia*, NRC, 2006.
- *Scientists, Engineers, and Track-Two Diplomacy: A Half-Century of U.S.-Russian Interacademy Cooperation*, NRC, 2004.
- *Partners on the Frontier: U.S.-Russian Cooperation in Science and Technology*, NRC, 1998.
- *Controlling Dangerous Pathogens: A Blueprint for U.S.-Russian Cooperation*, NRC/IOM, 1997.
- *An Assessment of the International Science and Technology Center*, NRC, 1996.
- *Dual-Use Technologies and Export Control in the Post-Cold War Era,* NRC, 1994.
- *Sustaining Excellence in Science and Engineering in the Former Soviet Union*, NRC, 1993.

- *Redeploying Assets of the Russian Defense Sector to the Civilian Economy*, NRC, 1993.
- *Reorientation of the Research Capability of the Former Soviet Union*, NRC, 1992.

BOOKS AND OTHER REPORTS

- Centers for Disease Control and Prevention, *CDC's Vision for Public Health Surveillance in the 21st Century,* MMWR 2012, 61 (Supplement, July 27, 2012).
- Can Russia Create a New Silicon Valley? *Economist,* July 14, 2012, p. 58.
- Eric Toner and Amesh Adalja, "Is H5N1 Really Highly Lethal?" *Biosecurity and Bioterrorism,* Volume 10, Number 2, 2012, Mary Ann Liebert, Inc., p. 224.
- Decree of the Chairman of the Government of the Russian Federation No. 1853p-P8, *Complex Program of Development of Biotechnology in the Russian Federation for the Period Until 2020*, April 24, 2012.
- *National Bioeconomy Blueprint*, Office of Science and Technology Policy, U.S. Government, April 2012.
- Bilateral Presidential Commission, U.S.-Russia, Joint Report, www.state/gov/russiabpc, 2012.
- *Annual Report of International Science and Technology Center*, Annual reports from 1994 to 2011, Moscow.
- *Foreign Operations Appropriated Assistance: Russia,* U.S. Department of State, Annual Report, 2011.
- Jason A. Rao, "U.S. Department of State's Biosecurity Engagement Program," *Encyclopedia of Bioterrorism Defense*, 2nd Edition, Wiley-Blackwell, 2011.
- Irina Dezhina, "State of Science, Technology, and Innovation Policy in Russia," Presentation at American Association for the Advancement of Science, April 2011.
- Matthew Rojansky, *Indispensable Institutions: The Obama-Medvedev Commission and Five Decades of U.S.-Russia Dialogue*, Carnegie Endowment for International Peace, Washington, 2010.
- Ernst and Young, *Doing Business in the Russian Federation,* Moscow, August 2010.
- *U.S. Assistance to Eurasia,* U.S. Department of State, Annual Reports, 2000–2010.
- David Hoffman, *The Dead Hand: The Untold Story of the Cold War and its Dangerous Legacy*, Anchor Books, 2009.
- Loren Graham and Irina Dezhina, *Science in the New Russia: Crisis, Aid, Reform*, Indiana University Press, 2008.

- Ministry of Health and Social Development and Russian Academy of Medical Sciences, *National Program for Influenza Pandemic Preparedness*, Moscow-St. Petersburg, 2006.
- Department of State, *Bioindustry Initiative*, Annual Program Report, 2005–2006, Washington, D.C., 2006.
- Roger Roffey, Wilhelm Unge, Jenny Clevestron, and Kristina S. Westerdahl, *Support to Threat Reduction of the Russian Biological Weapons Legacy—Conversion, Biodefence, and the Role of Biopreparat*, Institute of Defence Analysis, Stockholm, ISSN 1650-1942, April 2003.
- Amy Smithson, *Toxic Archipelago: Proliferation from the Former Soviet Chemical and Biological Weapons Complexes*, Henry L. Stimson Center, Washington, D.C., 1999.
- Glenn Schweitzer, *Experiments in Cooperation: Assessing U.S.-Russian Programs in Science and Technology,* Twentieth Century Fund and Century Foundation, 1997.

Appendix A.3

Organizations Consulted

RUSSIA-BASED ORGANIZATIONS

Russian Academy of Sciences

- Presidium
- Siberian Branch
- Institute of Chemical Biology and Fundamental Medicine
- Institute of Gene Biology
- Bakh Institute of Biochemistry
- Center for Bioengineering
- Grebenshchikov Institute of Silicate Chemistry
- Komarov Institute of Botany
- Ioffe Physical Technical Institute
- Engelhardt Institute of Molecular Biology
- Sechenov Institute of Evolutionary Physiology and Biochemistry
- Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry

Other

Federal Service in the Sphere of Consumer Rights Protection and Human Well-Being (Rospotrebnadzor)

Federal Medical Biological Agency

- Institute of Highly Pure Biopreparations

Russian Academy of Medical Sciences

- Institute of Experimental Medicine

- Chumakov Institute of Poliomyelitis and Viral Encephalitides

Research Institute of Influenza
Central Research Institute of Epidemiology
All-Russian Center for Molecular Diagnostics and Treatment
Joint Stock Company "InterLabService"
Russian Society of Biotechnology
Skolkovo Foundation
Rusnano
All-Russian Institute of Phytopathology, Academy of Agricultural Sciences
Vavilov Institute of Plant Industry, Ministry of Agriculture
Institute for Biomedical Problems
Moscow State University, Biology Department
Novosibirsk State University
International Science and Technology Center

UNITED STATES-BASED ORGANIZATIONS

Bilateral Presidential Commission
National Security Staff
Office of Science and Technology Policy
Department of State
Department of Defense

- Defense Threat Reduction Agency

Department of Energy

- United States Industry Coalition

Department of Health and Human Services

- Centers for Disease Control and Prevention
- National Institutes of Health
- Food and Drug Administration

Agricultural Research Service
Environmental Protection Agency
National Science Foundation
National Aeronautics and Space Administration
Fish and Wildlife Service
Agency for International Development
Civilian Research and Development Foundation
American Society for Microbiology
International Council on Life Sciences
Medtronic
Ely Lilly Company
U.S.-Russia Business Council
Carnegie Endowment for International Peace

Appendix B

Examples of U.S.-Russian Agreements of Special Relevance for Bioengagement

Agreement of September 9, 2012, concerning issuance of business, private, humanitarian, and tourist visas by Russia, issuance of B1/B2 visas by the United States, and issuance of visas for short-term official travel by both governments. (http://moscow.usembassy.gov/new-visa-agreement.html)

Agreement between the Government of the United States of America and the Government of the Russian Federation on Science and Technology Cooperation (with Annexes on (a) Establishment of a U.S.-Russian Joint Committee on Science and Technology and (b) Intellectual Property). Signed in 1993 for a 10-year duration, and extended for an additional 10 years in 2003.

Memorandum of Understanding between the Department of Health and Human Services and Ministry of Health and Social Development on Cooperation in Public Health and Medical Sciences. Signed in 2009 for an indefinite duration.

Memorandum of Understanding between the National Institutes of Health and the Russian Foundation for Basic Research of the Russian Federation (focused on joint HIV prevention studies). Signed in 2011 for an indefinite duration.

Protocol of Intent between the U.S. Centers for Disease Control and Prevention and the Federal Service for Surveillance on Consumer Rights Protection and Human Well-Being to Combat Communicable and Non-Communicable Diseases. Signed in 2012 for an indefinite duration.

Protocol of Intent between the U.S. Agency for International Development, the U.S. Department of Health and Human Services, and the Ministry of Health and Social Development on Cooperation for the Global Eradication of Polio. Signed in 2011 for a duration of 3 years.

Protocol of Intent between the U.S. Agency for International Development, the U.S. Department of Health and Human Services, and the Ministry of Health and Social Development on Cooperation in Combating Malaria. Signed in 2012 for a duration of 3 years.

Memorandum of Understanding between the National Institutes of Health, the National Academy of Sciences, the Institute of Medicine, the Russian Academy of Sciences, and the Russian Academy of Medical Sciences on Translational and Innovative Biomedical Research and Development of Pharmaceuticals. Signed in 2011 for a duration of 5 years.

Agreement between the U.S. National Academies and the Russian Academy of Sciences on Cooperation in Science, Technology, and Medicine. Signed in 2008 for a duration of 5 years.

Appendix C

Activities in Bioengagement of Selected U.S. Government Departments and Agencies

Appendix C.1

Department of State

Overarching Goal in Russia and Elsewhere: Work with governments and other stakeholders to build sustainable capacity for biosecurity, biosafety, disease surveillance, and cooperative scientific research.

1. Recent History of Department's Interests in Biosecurity Activities in Russia
   - Support of Nunn-Lugar Initiative: 1991
   - Biological Arms Control Activities: 1992 (continuation of earlier activities)
   - Policy/Program Direction of International Science and Technology Center (ISTC): 1994
   - Biotechnology Engagement Program: 1999
   - BioIndustry Initiative: 2002
   - Bioengagement Program: 2006 to present

2. Results of Emergency Appropriation of $30 million for BioIndustry Initiative Focused on Collaboration with Russia
   - Conversion of Sibbiopharm facility in Berdsk to commercial production of animal feed premixes, biopesticides, and enzymes for alcohol production.
   - Provision of U.S. government collateral guarantees for repayment of Russian bank loans to small Russian biotech enterprises.
   - Expanded U.S. interactions with components of the Biopreparat complex through the new organization TEMPO.
   - Support for commercialization-oriented activities at a number of Russian research institutes, including the upgrading to GLP and GMP standards.

- Support for influenza surveillance in Siberia.

3. Current Russia-related Activities of Special Interest
- Implications of planned withdrawal of Russia from ISTC: 2015
- Transfer of Russian components of ongoing bioengagement programs to Russian ownership, including responsibility for funding.
- Facilitation of connections of Russian scientists with international community.
- Encouragement of Russian support for broad international adoption of international biosecurity standards and guidelines.
- Development of long-term bioengagement strategy.

4. Lessons Learned from Bioengagement Activities with Russia and Other Countries
- Developing deep and broad relationships is critical.
- Partner government endorsement of engagement activities is essential.
- Communication strategies should focus on importance of public health capacity-building.
- Some states may be skeptical of U.S. objectives in promoting engagement activities.

5. Future for U.S.-Russia Partnership
- Identify new mechanisms for partnerships following Russia's withdrawal from the ISTC.
- Continue to jointly develop biological safety standards and programs in countries and regions of mutual interest.
- Support U.S. partnerships with Russian institutes for carrying out on a highly selective basis collaborative research and development activities.
- Collaborate to develop an open and transparent culture of responsibility among dual-use scientists.
- Strengthen detection and control of infectious diseases through collaboration.

SOURCE: Information provided by Department of State, October 2011 and July 2012.

Appendix C.2

Defense Threat Reduction Agency

The Defense Threat Reduction Agency (DTRA) began to expand bioengagement with Russian institutions in 1997. Initially, the focus was on eight pilot research projects, developed with the assistance of the U.S. National Academy of Sciences. These pilot projects were sited at the State Research Center for Virology and Biotechnology Vector (Koltsovo) and State Research Center for Applied Microbiology (Obolensk). A joint U.S.-Russian conference in Kirov during the development of the pilot projects broadened subsequent Russian participation in collaborative activities to include a number of other research institutions as well. At the outset, most of the Russian institutions were components of Biopreparat, a research-industrial complex, which was in the process of redirecting activities that had supported the Soviet-era biological defense program to civilian-oriented activities.

As of 2000, DTRA had committed more than $30 million to bilateral biology-related engagement activities. By 2011, the total commitment had increased to $71.2 million, although the annual commitments had steadily declined to about $1.5 million in 2011. Overall, about 9 percent of DTRA's global bioengagement program has been focused on Russia despite the much larger percentages in the early years. The activities supported in Russia have been primarily (a) research projects to characterize especially dangerous pathogens and to prevent and develop therapies for infections (see below) and (b) upgrades of security and safety conditions at selected Russian institutions, which handle large quantities of dangerous pathogens. Such upgrades have included consolidation of pathogens in secure areas, construction of fences around facilities, improved security at entry portals into laboratory complexes, and safety precautions within laboratories. While DTRA was interested for a number of years in working with Russian institutions to upgrade disease surveillance systems in Russian (the TADR program), this activity was not undertaken due to difficulties in reaching agreement on the details of proposals for cooperation.

By 2010, DTRA had shifted its emphasis to support of linkages of (a) U.S. universities and other institutions with (b) Russian universities and institutes. Recent projects have supported joint research to address topics such as the following:

- Mapping of the microbial biosphere.
- Relationship of plant pathogens and zoonotic pathogens.
- Understanding of persistent relationships between humans and pathogens.
- New applications of synthetic biology.
- Host response to infectious diseases.

Engagement over many years has benefited many scientists and institutions on both sides of the ocean. As to biosecurity/biosafety upgrades, visitors to Russian institutions that have participated in cooperative efforts have almost always commented positively on the much improved approaches to ensuring the security and safety throughout the institutions. As to research projects that have been fully implemented, U.S. partners give high marks to their Russian colleagues who have served as the project managers in various universities and institutes. The American participants have been generally pleased with opportunities to benefit from the work of Russian researchers, who have quickly mastered new techniques and produced results of considerable interest to the international scientific community.

DTRA has committed to continuing engagement with Russian organizations through pursuit of shared scientific interests, recognizing that key Russian ministries do not consider the Department of Defense a legitimate partner in addressing civilian biological concerns. DTRA plans to support activities of other U.S. organizations that are more acceptable partners. DTRA considers the following reasons as important motivation for U.S.-Russian engagement:

- Russia and U.S. cooperation in combating infectious diseases and potential bioterrorist acts sends a message of warning to potential terrorist groups.
- Transparency in research advances global progress toward dealing with infectious diseases and builds trust among countries.

DTRA has articulated the following characteristics of its future approaches:

- Engagement is to be based on cutting-edge research that responds to key scientific questions.

- Partnerships will engage leading U.S. scientists who will attract broad interest in collaborations.
- Science and scientific outcomes will drive bilateral dialogues and activities.
- Partnerships are in and of themselves a threat-reduction metric since they build mutual confidence and serve as verification mechanisms.
- New business models will be developed that are consistent with the needs of DTRA.

DTRA, working with Russian partners, developed the following metrics in 2008, which at times can be helpful in assessing biosafety and biosecurity efforts:

- Enhance capabilities to prevent theft.
    - Regulations
    - Biosafety guidelines
    - Facility plans
    - Biosafety and security standards
    - Biosafety and security upgrades at institutes
    - Biosecurity event notification
    - Biosafety event notification
- Enhance capabilities to detect events
    - Sharing of data on especially dangerous pathogens
    - Reporting laboratory results to responsible officials
    - Providing human-related reports to WHO
    - Providing animal-related reports to OIE
    - Sharing of case data
    - Reporting epidemiological data
    - Reporting laboratory results
    - Personal health data reported to WHO
    - Animal diseases reported to OIE
    - Investigations of incidents involving especially dangerous pathogens
    - Appropriate sample collection
    - Capabilities to diagnose especially dangerous pathogens
    - Strain characterization of plant pathogens
    - Appropriate sample transportation
- Sustainability
    - Testing of trainee test results
- Miscellaneous
    - Credible research results
    - Contribution to efforts of international scientific community
    - Biosafety guidelines

DTRA-SPONSORED RESEARCH PROJECTS IN RUSSIA

Genome of Monkeypox Virus (ISTC #884-2p) *State Research Center of Virology and Biotechnology Vector, Koltsovo*

Project Agreement Date: 10/8/99
Projected End Date: 10/8/01
Cost: $362,880

> **Key Findings:** A long-range PCR approach was used to construct clones for the complete genomes of different strains of pox viruses, including variola, to do comparative sequencing that establishes relationships among various viral forms. The work established that monkeypox is less related to variola than are other pox viruses, suggesting that the origin of the monkeypox disease is not related to smallpox.

Development of Liposomal Forms of IgAs for Prophylaxis and Treatment of Y. pestis (ISTC #1515) *State Research Center for Highly Pure Biopreparations, St. Petersburg*

Project Agreement Date: 08/01/02
Projected End Date: 10/31/05
Budget: $657,251

> **Key Findings:** Protection is provided to mice by aerosolized liposomal-delivered IgA antibodies directed towards the F1 antigen before challenge with 10^4 *Y. pestis*. No protection was observed if the aerosol was delivered after challenge.

Design of Experimental Aerosol DNA-vaccine Preparation against Hantaviral Infection (ISTC #1813) *Research Center for Toxicology and Hygienic Regulation of Biopreparations, Serpukhov*

Project Agreement Date: 06/01/01
Projected End Date: 07/31/05
Budget: $599,000

> **Key Findings:** Genes from small and medium segments of the hantaviral genome were cloned into plasmids. These plasmids were complexed with polyethylenimine (PEI) and delivered to mice in an aerosol form. Antibodies to the plasmid encoded antigens were measured. It was found that antibody

production was best against antigens from the medium segment and that the efficiency depended upon the presence of immunomodulators.

Genetic Identification of Crimean-Congo Hemorrhagic Fever (CCHF) Virus Isolates Circulating in Countries of the Region (ISTC #1291.2) *State Research Center of Virology and Biotechnology Vector, Koltsovo*

Project Agreement Date: 08/01/00
Projected End Date: 10/31/05
Budget: $604,645

Key Findings: A unique variable section in the genome encoded by the L-segment of CCHF was explored as a possible marker for geographically distinct isolates of the virus. The variable region was studied in 16 different isolates. The variable segment was found to encode a region between the main structural sequences involving the RNA-dependent RNA polymerase.

Studying the Role of *Yersinia pestis* Lipopolysaccharides Structural Organization in the Development of Immune Preparations (ISTC#1197) *Zelinsky Institute of Organic Chemistry, Moscow*

Project Agreement Date: 04/01/01
Projected End Date: 09/30/05
Budget: $943,408

Key Findings: This project has made major contributions to the understanding of the structures of lipopolysaccharide (LPS) structures and their biological activities. The work was the first to describe temperature dependent structural alterations in LPS structure that correlate with the bacterium's life in the insect vector and mammalian host. The investigators have developed a comprehensive data base on LPS and other glycostructure from the worldwide literature on this topic (**http://www.glyco.ac.ru/bcsdb/start.shtml).**

Immunofiltration and Immunoenzyme Express Diagnostic Test Kits for Determination of Infectious Diseases (ISTC #1233.2) *Research Center for Molecular Diagnostics and Therapy, Moscow*

Project Agreement Date: 03/01/00
Projected End Date: 08/31/05
Budget: $972,354

Key Findings: Presentation was made of a simple, fast, sensitive, and universal immunoassay method for detection of a broad range of infectious diseases, including diseases caused by agents with defense applications. The basis of this novel concept was microfiltration, using micro-column flow immunoassays using analytical markers of different types and nature as reporters. In the course of this project, novel monoclonal antibodies against unique epitopes biological warfare agents were developed, as well as a sensitive method of detecting uniform magnetic microspheres.

A Sampler for Detection and Express-Identification of Airborne Microorganisms and Implications for Counterterrorism (ISTC #1487) *Research Center for Toxicology and Hygienic Regulation of Biopreparations, Serpukhov*

Project Agreement Date: 07/01/00
Projected End Date: 03/31/06
Budget: $680,000

Key Findings: A unique sampler capable of collection and preservation of the viability of biological organisms from the air was designed, fabricated, and tested. The collector is based on a cyclone collector technology applied to a portable, personalized collector. Comparative testing of these devices has been carried out in the United States, and the results have proven the superiority of the design. DTRA's Visiting Scientist program has contributed significantly to the design and testing of these devices. Various detection technologies can also be adapted for use with the collectors.

Search for Antivirals for Treating and Prevention of Orthopoxviral Infections Including Smallpox (ISTC #1989) *State Research Center of Virology and Biotechnology Vector, Koltsovo*

Project Agreement Date: 3/01/01
Project End Date: 3/13/03
Buidget: $1,433,374 (co-funded with Department of Health and Human Services)

Key Findings: Utilization of the extensive chemistry capabilities in Russia and the coupling of this technology with the unique testing facilities at Vector have resulted in the identification of a collection of new compounds that show antiviral activities when tested against pox viruses. These compounds are being evaluated in the United States against variola viruses. A movie of an expedition into Northern Siberia to collect smallpox samples from the bodies of people suspected of death from smallpox was developed. Such expeditions have resulted in a number of samples that contained DNA, but no viable viruses.

Combinatorial Antibody Libraries of Orthopoxviruses (ISTC #1638) *State Research Center of Virology and Biotechnology Vector, Koltsovo*

Project Agreement Date: 9/05/01
Project End Date: 9/05/03
Budget: $217,296 (co-funded with Department of Health and Human Services)

Key Findings: Project resulted in a new phage display combinatorial library derived from the lymphocytes of an individual vaccinated with vaccinia virus. The new library contained phage, which showed different reactivities to vaccinia, cowpox, and ectromelia viruses. These antibodies were thus species-specific. Neutralization tests were carried out with these antibodies, and they were shown to be positive. In addition, these antibodies are active in western blots allowing the identification of specific targets for these phage displayed humanized antibodies.

Conservation of Genetic Material and Study of Genomic Structure of Different Variola Virus Strains (ISTC #1987) *State Research Center of Virology and Biotechnology Vector, Koltsovo*

Project Agreement Date: 3/01/01
Project End Date: 6/13/03
Cost: $1,336,913 (co-funded with Department of Health and Human Services)

Key Findings: This project has made major contributions to understanding the interrelationships of different pox viruses. The eradication of smallpox as a disease of concern has left the medical community with the question as to whether this virus could reemerge from another pox virus. Also, questions about the recent appearance of monkey pox virus as a potential human disease has added to this concern. Comparative sequence studies performed by Vector and Centers for Disease Control scientists have shown that the large number of sequence differences between variola and monkey pox suggest that emergence of a smallpox-type disease from monkey pox is not likely. Variola is, in fact, more closely related to other pox viruses, such as camel pox.

Magnetometric Immunosensor for Multi-Pathogen Continuous Monitoring (ISTC #2129) *Research Center for Molecular Diagnostics and Therapy, Moscow*, and *Institute of Physics, Moscow Medical Academy*

Project Agreement Date: 08/01/05
Projected End Date: 07/31/2007
Budget: $496,906

Key Findings: This project developed a magnetometric immunosensor for detection of three pathogens and one toxin: *B. anthracis*, *Y. pestis*, *F. tularensis* and *Clostridium botulinum* toxin A. This detection system is portable and has increased sensitivity and speed over conventional detection techniques. The system has been field tested for environmental sampling.

Upgrade of the Security and Safety Systems to Protect Biological Material at the All-Russian Research Institute of Phytopathology (ISTC #2685) *All-Russia Scientific Research Institute for Phytopathology* (*VNIIF), Russian Academy of Agricultural Sciences*

Project Agreement Date: 09/01/04
Projected End Date: 06/30/13
Budget: $2,929,404.91

Key Findings: This project has made major contributions in providing a safer and more secure working environment for VNIIF scientists, researchers, and visitors, ensuring that phytopathogens and the specialists who work with them are properly protected, along with protection of the environment. The research aspect of this project has contributed to determinations of the pathogenic and toxic properties of collection strains of fungi responsible for barley and wheat Root Rot, Snow Mold, and Fusarium Head Blight, which could negatively impact Russia's food and agriculture industries.

NOTE: Other DOD components such as DARPA, have also supported bioengagement. Information provided by DTRA and ISTC, February 2012.

Appendix C.3

Department of Energy

Since 1994, the National Nuclear Security Administration's Global Initiatives for Proliferation Prevention (GIPP) and its predecessor programs within the Department of Energy have engaged Russian scientists with experience in the defense sector and other technical specialists in civilian activities aimed at advancing global security and nonproliferation objectives. The program has financed more than 100 projects at a cost of $40–45 million in the biosciences in Russia. In 2011, funding levels were at or near their lowest level since the program began. Examples of projects that the department considered successful are set forth below.

Project: Microbial Diversity for Novel Biotechnology Applications
Russian and Other Partner Institutes:
Institute for Volcanology and Seismology, Russian Academy of Sciences Far-East Branch, Petropavlovsk-KamchatkaCenter for Ecological Research and BioResources Development, Pushchino Durmishidze Institute for Biochemistry and Biotechnology, Tbilisi, Georgia Institute for Microbiology, National Academy of Sciences of Uzbekistan, Tashkent, Uzbekistan
U.S. Industry Partner:
Diversa Corporation, San Diego, California

The project established a multiyear program of rational bioprospecting on the Kamchatka Peninsula. Environmental samples were exported to the United States by the Center for Ecological Research and BioResources Development to the industrial partner, Diversa Corporation. This multiyear program resulted in a large number of novel microorganisms that were later screened by Diversa researchers, a number of which were used in other GIPP projects that target transgenic plant generation for crop protection. Diversa's most successful product was the laccase enzyme that it sold to the paper pulp industry to replace bleach in whitening of paper pulp.

Project: Development of Recombinant Luciferase and Related Reagents for Portable Photometric Reagents
Russian Institutes:
Gamaleya Institute of Epidemiology and Microbiology, Moscow
Moscow State University
Industry Partner:
New Horizon Diagnostics Corp. (NHD)

The project resulted in the establishment of the company Lumtek LLC in 2004. Lumtek was tasked by NHD to improve current bioluminescence-based detector hardware and reagents for a range of commercial detectors. Lumtek successfully designed and manufactured a new Russian Luminometer. Lumtek continues to manufacture test systems, including a Luminometer device and reagents for biocontamination express control for customers in Russia, Ukraine, and France. The target markets are food industry, ecology, and medicine. In May 2012, NHD initiated quality control and assurance procedures of the Lumtek reagents and Luminometers. If successful, Lumtek plans to sell its products to NHD, and NHD will market them in the United States. NHD would like to contract with Lumtek for production of at least 100,000 test systems and 100–300 Luminometers per year.

Combined Projects: Development of Microbiological Methods for Oil Pollution Decontamination in Soil and Water Surface and Symbiont—Plant Growth Regulator
Russian Institute:
JSC Biochimmash
Industry Partner:
Dye Seed Ranch Inc.

An oil biodegradant prep was developed and successfully tested in Montana during this 3-year project. Dye Seed supported the trials conducted by Biochimmash in Siberia and other parts of Russia and reported the results of the trials to the Montana Gas and Oil Committee. Under the Plant Growth Regulator project, Biochimmash developed a plant growth accelerator that shortens the cultivation period of agricultural products and grass. After successful completion of the project, Biochimmash renovated the pilot production facility to manufacture the oil-degrading prep and plant growth accelerator (entitled MICEFIT). After renovation, the pilot plant became the spin-off company Bioprogress that leases the facility and equipment from Biochimmash. Bioprogress produces the oil biodegradant and plant growth accelerator and sells it to oil-production companies and farmers. Bioprogress produces other natural compounds as well. Bioprogress's revenue has been steadily growing since 2006. Recently, Biochimmash received an invitation from NineSigma Inc. (Cleveland, Ohio) to submit a proposal for cultivation technologies that shorten the cultivation period of agricultural products.

Project: Development of Effective Decontamination Methods and Technology
Russian Institute:
Institute of Highly Pure Biopreparations
Research Institute of Influenza
Industry Partner:
Isonics

Under this project, the biodecontamination method entitled PAEROSOL was developed. Two patents are pending. The Defense Threat Reduction Agency (DTRA) sponsored the validation of PAEROSOL at the Madigan Army Medical Center for its effectiveness in the decontamination of hospital pathogens that cause cross-contamination of patients and result in high morbidity and mortality. Estimates of the resulting costs to deal with hospital infections range from $4.5 billion to $11 billion annually. The validation was successful. A U.S. laboratory is developing a proposal to apply PAEROSOL for the decontamination of military vehicles, cargo, etc., that are returned from Afghanistan and the other military theaters. PAEROSOL will ensure appropriate disinfection to prevent transmission of dangerous human, animal, and plant pathogens to the United States. According to specialists at Cornell University, importation of invasive species costs the United States more than $138 billion each year.

Project: Antibody-Based Diagnostics and Production for High Consequence Animal Pathogens
Russian and Other Partner Institutes:
Russian State Diagnostic and Prevention Center for Human and Animal Diseases (DPC)
Ivanovsky Virology Institute
All-Russia Institute for Animal Health
Institute of Experimental and Clinical Veterinary Medicine of the Ukrainian Academy of Agricultural Sciences
Gamaleya Institute of Epidemiology and Microbiology
Industry Partner:
New Horizon Diagnostics (NHD)

This project produced novel antigen and monoclonal systems capable of detecting an array of high-consequence animal pathogens including foot-and-mouth disease (FMD), African swine fever, H5N1 avian influenza, and prion diseases, among others. Three invention disclosures and one patent application were filed for novel reagents capable of diagnosing Porcine Respiratory and Reproductive Syndrome (PRRS), FMD, and prion diseases. The diagnostic kits and treatments being jointly developed and marketed by DPC and NHD are antibody based and designed to handle food and environmental matrices as well as antibody and enzyme treatments for animal diseases. DPC is also producing and marketing the reagents for diagnosing several diseases in Russia through a partnership with NARVAC, Inc. (Russia). NHD has received funding from the U.S. Pork Producers Association to complete development and validation of a diagnostic kit for PRRS.

Project: Fluorinated Analogs of Bioactive Garlic Components
Russian Institute:
State Research Institute of Organic Chemistry and Technology (SRIOCT)
Industry Partner:
LifeTime Pharmaceuticals

The focus of the project was to develop novel anticancer agents from garlic extracts and individual components known to exert a pronounced cytotoxic activity against malignant cells. The SRIOCT team designed and synthesized over 60 garlic analogs. Four were eventually selected for further development by SRIOCT and the commercial partner in collaboration with the U.S. National Cancer Institute, because they are stable and easily synthesized and demonstrated high antitumor activity. The project yielded four invention disclosures.

Project: Anti-Cytokine Antibodies: Immune-Mediated Disease
Russian Institutes:
Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry
State Institute of Genetics
Institute of Highly Pure Biopreparations
Russian Research Center for Molecular Diagnostics and Therapeutics
Industry Partner:
Advanced Biotherapy Concepts, Inc. (ABCI)

In this project, genetically engineered monoclonal antibodies were used to address efficacy and reactivity issues associated with antibody-based therapies, the rationale being that humanized antibody-based therapies would reduce severe immune reactions during repeated treatment, thereby increasing the life of the therapy when compared to mouse-based therapy systems. This project resulted in four invention disclosures. ABCI has sold its patent portfolio for proprietary antibody treatments that remove or neutralize certain interferons and other key cytokines induced by alpha interferon to another U.S. company that is currently negotiating with SOI and a national laboratory regarding further product development and clinical trials.

Project: Antibody-Based Diagnostics
Russian Institutes:
Russian Research Center for Molecular Diagnostics and Therapeutics (RCMDT)
Russian State Diagnostic and Prevention Center for Human and Animal Diseases (DPC)
Gamaleya Institute of Epidemiology and Microbiology
State Research Center for Applied Microbiology (SRCAM)
Industry Partner:
New Horizon Diagnostics (NHD)

The project produced novel antigen and monoclonal systems capable of detecting an array of high-consequence pathogens, including anthrax, plague, tularemia, *E. coli*, *Salmonella*, and botulinum toxin, among others. Two patent applications were filed for novel reagents capable of detecting *E. coli* and botulinum toxins. The diagnostic kits being jointly produced and marketed by RCMDT, DPC, and NHD in Russia and the FSU are antibody-based and designed to handle food and environmental matrices. Test kits for anthrax, plague, and tularemia were independently validated by SRCAM. RCMDT is also producing and marketing these reagents in Russia and the European Community through joint stock companies in which the principle investigator maintains a business interest. NHD has received funding from the Department of Defense and Environmental Protection Agency to continue development of kits for biodefense and food and water safety applications, respectively.

United States Industry Coalition

Since 1994, GIPP and its predecessor organizations have also worked with the United States Industry Coalition (USIC) to direct investment toward Russia as well as other states that emerged from the USSR. The mission has been to engage Soviet-era defense scientists and engineers in sustainable and gainful civilian work. Over 150 U.S. companies have worked with 110 institutes in Russia, Georgia, Uzbekistan, Armenia, Kazakhstan, and the Ukraine, with investments totaling over $280 million—approximately a third of this applied within the biological sciences. Investments are profit driven, with profits accruing for both participants. These projects have resulted in diverse commercial successes at impressive rates, including efforts in the fields of radioisotope medical therapy, rapid diagnostics, drug development, crop projection, biodecontamination, vaccine delivery, and wound healing.

USIC reports that the projects related to the biological sciences are estimated to have had the following impacts:

- Created over 700 sustained jobs.
- Generated over $70 million in revenue for U.S. and FSU companies.
- Attracted approximately $100 million in outside investment.
- Created or sustained approximately a dozen independent and joint U.S.-FSU businesses.

- Resulted in over 30 U.S., Russian, and other patent applications.
- Achieved a 25 percent commercialization rate, with a further 24 percent resulting in substantial business achievements (e.g., royalties, grants, investment, etc.)
- Approximately 30 projects resulted in follow-on activity.

These early achievements are indicative of the impact of the program in bringing technological developments to commercially successful endpoints.

The United States Industry Coalition has identified a few challenges for moving forward with this work, namely adaptation to an evolving Russia and developing viable cost-sharing models. Quantifying and valuing cost-sharing are also challenging.

SOURCE: Information provided by Department of Energy, February 2012.

Appendix C.4

Department of Health and Human Services (Biotechnology Engagement Program)

Projects facilitated by the International Science and Technology Center included the following:

Production and Specific Properties of IgA Protease Secreted by Neisseria Meningitidis (ISTC No. 0631-2p) *State Research Center for Applied Microbiology and Biotechnology, Obolensk, Moscow region*
Project Agreement Date: 07/01/2003
Projected End Date: 03/24/2009
Budget: $312,307

Study of the Genetic and Serologic Diversity of Hantaviruses in the Asian Part of Russia (ISTC No. 0805-2p) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region, Institute of Systematics and Ecology of Animals, Novosibirsk, Khabarovsk Antiplague Station, Khabarovsk*
Project Agreement Date: 01/01/2007
Projected End Date: 10/08/2010
Budget: $392,650

The Study of Prevalence, Genotype Distribution and Molecular Variability of Isolates of Hepatitis C Virus in the Siberian Part of Russia (ISTC No. 1637) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region*
Project Agreement Date: 10/01/2000
Projected End Date: 04/19/2006
Budget: $692,768

Combinatorial Antibody Libraries to Orthopoxviruses (ISTC No. 1638) *State Research Center of Virology and Biotechnology Vector/Research Institute of Bioengineering, Koltsovo, Novosibirsk region*

Project Agreement Date: 08/01/2001
Projected End Date: 07/15/2011
Budget: $227,294 (cofunded with Defense Threat Reduction Agency)

Drug-resistant Strains of M. Tuberculosis: Genetic Analysis (ISTC No. 1642) *State Research Center for Applied Microbiology, Obolensk, Moscow region*

Project Agreement Date: 10/01/2000
Projected End Date: 04/16/2003
Budget: $102,500

Development and Certification of National Reference and Control Hbsag Serum Panels for Evaluating the Quality of Hepatitis B Diagnostics in Russia (ISTC No. 1803) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk reg., Tarasevich State Standardization and Control of Medical Preparations Research Institute, Moscow*

Project Agreement Date: 10/01/2002
Projected End Date: 02/07/2007
Budget: $351,320

Comparative Mycobacterial Genomics: Unraveling Differences of Functional and Diagnostic Importance by Subtractive Hybridization (ISTC No. 1845) *State Research Center for Applied Microbiology, Obolensk, Institute of Bioorganic Chemistry, Moscow*

Project Agreement Date: 10/01/2000
Projected End Date: 03/13/2003
Budget: $105,000

Development of Technology for Production of Nutrient Media for Isolation and Drug Susceptibility Testing of M. Tuberculosis (ISTC No. 1846) *State Research Center for Applied Microbiology, Obolensk*

Project Agreement Date: 10/01/2000
Projected End Date: 11/13/2003
Budget: $242,000

Development of Legal, Organizational and Scientific Concept for the Establishment of the International Center for the Study of Emerging and Reemerging Infectious Diseases (ICERID) at the State Research Center of Virology and Biotechnology Vector (ISTC No. 1884) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region*

Project Agreement Date: 10/01/2000
Projected End Date: 04/19/2005
Budget: $271,262

Epidemiology of Drug-Resistant Tuberculosis in Western Siberia: Determining the Distribution and Genetic Characteristics of Drug-Resistant Mycobacterium Tuberculosis Isolates in the Novosibirsk Oblast (ISTC No. 1980) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk reg., Boreskov Institute of Catalysis/Novosibirsk Institute of Bioorganic Chemistry, Akademgorodok, Novosibirsk region*
Project Agreement Date: 01/01/2002
Projected End Date: 01/16/2008
Budget: $445,000

Conservation of Genetic Material and Study of Genomic Structure of Different Variola Virus Strains (ISTC No. 1987) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region*
Project Agreement Date: 03/01/2001
Projected End Date: 07/15/2011
Budget: $1,336,913 (cofunded with the Defense Threat Reduction Agency)

Search for Antivirals for Treating and Prevention of Orthopoxviral Infections Including Smallpox (ISTC No. 1989) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region, Engelhardt Institute of Molecular Biology, Moscow, Ural State Technical University, Ekaterinburg*
Project Agreement Date: 03/01/2001
Projected End Date: 07/15/2011
Budget: $1,368,362.05 (cofunded with the Defense Threat Reduction Agency)

Biochip Application in TB Diagnostics for Fast Discrimination and Strain Typing of Multidrug-Resistant Tuberculosis in Russia (ISTC No. 2019) *Engelhardt Institute of Molecular Biology, Moscow, State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region*
Project Agreement Date: 04/01/2001
Projected End Date: 11/9/2005
Budget: $678,000

The Development and Application of Methods to Control Emergent/Re-emergent Vector-Borne Diseases in Russia and the USA with Special Attention to West Nile Encephalitis (ISTC No. 2087) *Ivanovsky Institute of Virology, Moscow, Central Research Institute of Epidemiology, Moscow, State*

Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region

Project Agreement Date: 10/01/2001
Projected End Date: 04/27/2006
Budget: $1,051,365

Development of Rabies Control System in Wild Carnivora and Stray Dogs in the Russian Federation (ISTC No. 2090) *Pokrov Plant of Biopreparations, Pokrov, Vladimir region*

Project Agreement Date: 07/01/2004
Projected End Date: 05/20/2009
Budget: $618,520

Designing, Engineering and Biological Testing of Multi-CTL Epitope-Based DNA Vaccine Against HIV-1 (ISTC No. 2153) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region*

Project Agreement Date: 10/01/2002
Projected End Date: 12/21/2005
Budget: $257,458

Diversity of Strains of Measles and Mumps Viruses in Russia (ISTC No. 2168) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region*

Project Agreement Date: 01/01/2002
Projected End Date: 01/16/2008
Budget: $1,317,400

Synthesis, Characterization of Targeted Delivery to Macrophage Receptors and Evaluation of Anti-Tubercular Activity of the Conjugates of Anti-Tubercular Antibiotics with Ligands to Macrophage (ISTC No. 2174) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region, Novosibirsk Institute of Tuberculosis, Novosibirsk*

Project Agreement Date: 10/01/2002
Projected End Date: 07/08/2006
Budget: $450,000

A Therapeutic Autologous HIV Vaccine on the Basis of a Membranitropic Preparation and the HIV-1/2 Strain in the HIV Patient (ISTC No. 2175) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region*

Project Agreement Date: 01/10/2001
Projected End Date: 02/15/2006
Budget: $330,000

Mycobacterium Tuberculosis Cytokines: Structure and Role in Tuberculosis Latency (ISTC No. 2201) *State Research Center for Applied Microbiology and Biotechnology, Obolensk, Moscow region, Russian Academy of Sciences/A. N. Bach Institute of Biochemistry, Moscow*
Project Agreement Date: 10/01/2002
Projected End Date: 02/12/2008
Budget: $700,000

Characterizations and Comparisons of Bartonella Strains of Animal and Human Origins from Russia and the USA (ISTC No. 2223) *Gamalei Institute of Epidemiology and Microbiology, Moscow, Moscow Medical Academy, Moscow*
Project Agreement Date: 10/01/2003
Projected End Date: 11/21/2008
Budget: $490,000

Comparative Mycobacterial Genomics: Unraveling Differences of Functional and Diagnostic Importance by Subtractive Hybridization (ISTC No. 2225) *State Research Center for Applied Microbiology and Biotechnology, Obolensk, Moscow reg., Institute of Bioorganic Chemistry, Moscow*
Project Agreement Date: 10/01/2001
Projected End Date: 11/10/2006
Budget: $468,372

Catalytic Antibody Approach in Development of New Antiviral Therapeutics (ISTC No. 2226) *Institute of Bioorganic Chemistry, Moscow, State Research Center for Applied Microbiology and Biotechnology, Obolensk, Moscow region*
Project Agreement Date: 07/01/2003
Projected End Date: 04/18/2012
Budget: $576,827

Construction of Recombinant Plasmids Encoding Synthesis of Pathogenic Microorganism Protective Antigens and Study of Their Properties (ISTC No. 2237) *State Research Center for Applied Microbiology and Biotechnology, Obolensk, Moscow region*
Project Agreement Date: 04/01/2002
Projected End Date: 01/10/2008
Budget: $596,550

Integrated Preclinical/Clinical Aids Vaccine Development (ISTC No. 2344) *Institute of Highly Pure Biopreparations, St. Petersburg*
Project Agreement Date: 10/01/2002
Projected End Date: 09/25/2006
Budget: $710,000

Development of a Candidate Vaccine Capable of Eliciting Protective Humoral and Cell-Mediated Responses to a Broad Range of HIV-1 Variants (ISTC No. 2450) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region, Institute of Highly Pure Biopreparations, St. Petersburg*

Project Agreement Date: 10/01/2002
Projected End Date: 03/11/2008
Budget: $468,822

Surveillance on Prevalence and Molecular Mechanisms of Antimicrobial Resistance Among Streptococcus Pneumoniae in Russia Federation (ISTC No. 2460) *State Research Center of Antibiotics, Moscow*

Project Agreement Date: 04/01/2004
Projected End Date: 04/29/2008
Budget: $380,000

Anti-Influenza Virus Therapeutic (ISTC No. 2464) *Institute of Bioorganic Chemistry, Moscow State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region*

Project Agreement Date: 01/01/2003
Projected End Date: 06/16/2008
Budget: $817,425

Development of Oligonucleotide Microchips for Diagnostic of Human-Pathogenic Orthopoxviruses (ISTC No. 2508) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk reg., Engelhardt Institute of Molecular Biology, Moscow*

Project Agreement Date: 10/01/2002
Projected End Date: 04/14/2008
Budget: $849,668

The Study of Vilyui Encephalomyelitis: Identification of the Etiologic Agent; Peculiarities of Epidemiology and Prophylaxis (ISTC No. 2539) *Institute of Clinical Immunology, Novosibirsk, Research Institute of Epidemiology and Microbiology, Irkutsk, State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region*

Project Agreement Date: 04/01/2004
Projected End Date: 08/27/2008
Budget: $394,345

Candidate DNA-Vaccines against HIV (ISTC No. 2547) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region*

Project Agreement Date: 04/01/2003
Projected End Date: 07/25/2007
Budget: $341,250

Study of Heat Shock Protein Functions in Lymphoid Cell Populations (ISTC No. 2627)
Institute of Bioorganic Chemistry, Moscow, State Research Center for Applied Microbiology and Biotechnology, Obolensk, Moscow region
Project Agreement Date: 01/01/2004
Projected End Date: 10/22/2010
Budget: $669,936

Tuberculosis in Central Russia: Genetic Peculiarities of the Pathogen and Drug Resistance in Mycobacterium Tuberculosis (ISTC No. 2628) *State Research Center for Applied Microbiology and Biotechnology, Obolensk, Moscow region*
Project Agreement Date: 01/01/2005
Projected End Date: 06/24/2008
Budget: $251,380

Molecular Mechanisms of Ganglioside-Induced Apoptosis of T-Lymphocytes (ISTC No. 2654)
Institute of Bioorganic Chemistry, Moscow, Institute of Immunological Engineering, Lyubuchany, Moscow region
Project Agreement Date: 01/01/2004
Projected End Date: 07/12/2012
Budget: $584,028

Test-Kit for Rapid Drug Susceptibility Testing of M. Tuberculosis (ISTC No. 2748) *State Research Center for Applied Microbiology and Biotechnology, Obolensk, Moscow region*
Project Agreement Date: 04/01/2004
Projected End Date: 10/6/2010
Budget: $474,600

Association of Human Lymphocyte Receptors with Membrane Lipid Rafts: Implications for Development of Anti-HIV Therapies (ISTC No. 2812) *Institute of Immunology, Moscow*
Project Agreement Date: 10/01/2004
Projected End Date: 07/02/2008
Budget: $270,000

Application of Tritium Bombardment Technique to Uncover the Structure of M1 Protein of Influenza Virus, M1-Hemagglutinin Interactions and Their Role in Viral Entry (ISTC No. 2816) *Semenov Institute of Chemical Physics, Moscow, Institute of Bioorganic Chemistry, Moscow, Moscow State University/ A.N. Belozersky Institute of Physical and Chemical Biology, Moscow*

Project Agreement Date: 04/01/2004
Projected End Date: 08/04/2008
Budget: $559,970

Investigation of Analytical Approaches to Determine the Authenticity/Quality of Pharmaceutical Products to Improve the Public Health by Identifying Counterfeit and Ineffective Products (ISTC No. 2829) *Moscow State University, Department of Chemistry, Moscow*
Project Agreement Date: 04/01/2004
Projected End Date: 07/16/2008
Budget: $471,033

Development of a Research Center for Tuberculosis Clinical Trials Through the Conduct of a Study of a Modified Treatment Regimen for WHO Category 1 Patients (ISTC No. 2879)
The First Moscow State Medical University named after I.M. Sechenov/Research Institute of Phthisiopulmonology, State Research Center for Applied Microbiology and Biotechnology, Obolensk, Moscow region
Project Agreement Date: 04/01/2005
Projected End Date: 06/05/2011
Budget: $1,369,509

Elaboration of Efficient Methods for Preparation of a Hepatitis A Virus Antigen on the Basis of a Non-Primate Cell-Adapted IVA Strain for Diagnostic and Prophylactic Purposes (ISTC No. 2899) *Research Center of Molecular Diagnostics and Therapy, Moscow*
Project Agreement Date: 01/01/2005
Projected End Date: 07/25/2008
Budget: $346,500

Biochips for Early Diagnostics of HIV and Hepatitis B and C Viruses in Donor Blood (ISTC No. 2906) *Engelhardt Institute of Molecular Biology, Moscow*
Project Agreement Date: 04/01/2005
Projected End Date: 07/21/2008
Budget: $399,862

Spread and Molecular Mechanisms of Resistance to Beta-Lactam Antibiotics Among Gram-Negative Bacteria in Nosocomial Infections (ISTC No. 2913)
Moscow Medicine Academy, Moscow, State Research Center for Applied Microbiology and Biotechnology, Obolensk, Moscow region
Project Agreement Date: 01/01/2005
Projected End Date: 06/17/2009
Budget: $677,964

Molecular Identification of Rubella Virus Isolates Circulating in the West Siberia (ISTC No. 2924) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region*
Project Agreement Date: 01/01/2004
Projected End Date: 03/31/2008
Budget: $297,055

The Epidemiology of Viral Gastroenteritis in Russia. Development of New Assays for Virus Detection and Characterization (ISTC No. 2935) *Central Research Institute of Epidemiology, Moscow, State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region*
Project Agreement Date: 01/01/2005
Projected End Date: 08/27/2010
Budget: $683,275

Antidotes to Highly Toxic Organophosphates (ISTC No. 2951) *Institute of Toxicology, St. Petersburg*
Project Agreement Date: 04/01/2004
Projected End Date: 05/13/2005
Budget: $27,500

Further Improvement of Influenza Surveillance in Russia. Contribution in Global Influenza Pandemic Preparedness (ISTC No. 3070) *Research Institute of Influenza, St. Petersburg, Ivanovsky Institute of Virology, Moscow*
Project Agreement Date: 04/01/2006
Projected End Date: 02/29/2012
Budget: $1,702,922

Phosphorescence Multianalyte Microanalysis of Dried Blood Spots as a Basis of Seroepidemiological Monitoring of Zoonotic Infections Transmitted by Ixodid Ticks (ISTC No. 3135) *State Research Institute of Biological Instrument-Making, Moscow, Close Joint Stock Company "Immunoscreen," Moscow*
Project Agreement Date: 11/01/2005
Projected End Date: 04/22/2011
Budget: $665,550

Establishing Meaningful Critical Concentrations of 2-nd Line Anti-TB Drugs for in Vitro Susceptibility Testing Based on in Vivo Efficacy in Animal Models (ISTC No. 3139)
State Research Center for Applied Microbiology, Obolensk, Moscow region
Project Agreement Date: 02/01/2007
Projected End Date: 01/25/2012
Budget: $651,930

The Role of Ixodes Persulcatus' Saliva in Lyme Disease Immunopathogenesis (ISTC No. 3171) *State Research Center for Applied Microbiology and Biotechnology, Obolensk, Moscow region*

Project Agreement Date: 10/01/2005
Projected End Date: 11/01/2012
Budget: $790,000

Computer-Assisted Discovery of New HIV-1 Integrase Inhibitors (ISTC No. 3197)
Institute of Biomedical Chemistry, Moscow; Institute of Organic Chemistry, Moscow; Moscow State University/A.N. Belozersky Institute of Physical and Chemical Biology, Moscow

Project Agreement Date: 04/01/2005
Projected End Date: 09/13/2010
Budget: $569,759

Immunologic and Structural Studies on Mammalian Cell Expressed Recombinant HCV Envelope Proteins E1 and E2 (ISTC No. 3255) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk region*

Project Agreement Date: 02/01/2006
Projected End Date: 04/05/2011
Budget: $540,637

Genetic Diversity of HIV-1 Circulating on the Territory of Russia (ISTC No. 3277) *Scientific Research Institute of Vaccines and Serums, Moscow, Central Research Institute of Epidemiology, Moscow*

Project Agreement Date: 02/01/2006
Projected End Date: 09/06/2012
Budget: $616,075

Implication of the Universal PCR on Bacterial 16S Ribosomal RNA in the Blood Service and in Clinical Microbiology (ISTC No. 3359) *Research Center of Toxicology and Hygienic Regulation of Biopreparations, Serpukhov, Moscow region, Ministry of Health/Blood Center, Moscow, The First Moscow State Medical University named after I.M. Sechenov, Moscow*

Project Agreement Date: 01/01/2007
Projected End Date: 12/01/2012
Budget: $481,675

Improvement and Standardization of Laboratory and Epidemiologic Rubella Surveillance Methods in Russian Federation (ISTC No. 3373) *Scientific Research Institute of Vaccines and Serums, Moscow, Research Institute of Influenza, St. Petersburg*

Project Agreement Date: 09/01/2006
Projected End Date: 05/18/2012
Budget: $350,145

Collection and Analysis of the Information, Creation of the Computer Database on Radioactive Contamination of Environments in Russia, Belarus and Ukraine at the Early Phase of the Chernobyl Accident (ISTC No. 3452) *Scientific and Production Association "Typhoon," Obninsk, Kaluga region*
Project Agreement Date: 11/01/2006
Projected End Date: 03/27/2009
Budget: $100,000

Development and Certification of National Reference and Control Anti-HCV Antibodies Serum Panels for Evaluating the Quality of Hepatitis C Diagnostics in Russia (ISTC No. 3526) *State Research Center of Virology and Biotechnology Vector, Koltsovo, Novosibirsk reg., Tarasevich State Standardization and Control of Medical Preparations Research Institute, Moscow*
Project Agreement Date: 04/01/2007
Projected End Date: 08/14/2012
Budget: $471,737

Salmonella Surveillance in Russian Federation (ISTC No. 3533) *Central Research Institute of Epidemiology, Moscow*
Project Agreement Date: 01/01/2007
Projected End Date: 07/11/2012
Budget: $327,550

Development of an Oligonucleotide Microarray Chip for Typing Various Subtypes of Type A Influenza Virus (ISTC No. 3803) *Siberian Branch of RAS/Institute of Chemical Biology and Fundamental Medicine, Novosibirsk*
Project Agreement Date: 11/01/2007
Projected End Date: 12/01/2012
Budget: $360,000

Development of a Rapid Test for Clinical Laboratory Diagnosis of Chlamydia Trachomatis (ISTC No. 3846) *Saratov Scientific and Research Veterinary Institute, Saratov*
Project Agreement Date: 08/01/2008
Projected End Date: 12/31/2013
Budget: $248,130

Analysis of T-cell Differentiation Status and the Development of a New Immunological Approach for Active TB Diagnosis and Monitoring (ISTC No. 4072) *Central Tuberculosis Research Institute, Moscow*

Project Agreement Date: 06/01/2011
Projected End Date: 08/26/2012
Budget: $10,000

SOURCE: Information provided by ISTC, March 2012.

Appendix C.5

National Institutes of Health

From 2006 to 2011, the annual investments of the National Institutes of Health (NIH) in research at Russian institutions averaged approximately $6.2 million (see Figure C.5-1). The level is declining and represents only 2–3 percent of the overall level of NIH awards to scientists abroad. The areas of research have included drug and alcohol abuse, HIV, radiation exposure, tuberculosis, cardiovascular diseases, demographics, genetics, and basic research. In addition, many Russian researchers have participated in the NIH intramural visiting program, with about 100 visitors during 2010. In addition, more than 100 Russian trainees have been supported since 2000, with the majority working in the field of infectious disease research.

In addition, NIH and its National Institute of Allergy and Infectious Diseases have managed the BioTechnology Engagement Program (BTEP) supported by the Department of State (see Appendix C.4). During fiscal year 2011, seven BTEP projects were active. These and previous projects focused on:

- High-impact and emerging infectious diseases: tuberculosis, HIV, hepatitis, plague, and influenza.
- Endemic and other infectious diseases: rubella, rabies, *helicobacter pylori*.
- Vector, food, and water-borne diseases.

In November 2009, NIH, together with the National Academy of Sciences and the Institute of Medicine, signed an agreement with the Russian Academy of Sciences. This agreement led to the development of a public-private partnership coordinated by the Foundation for the National Institutes of Health. The partner-

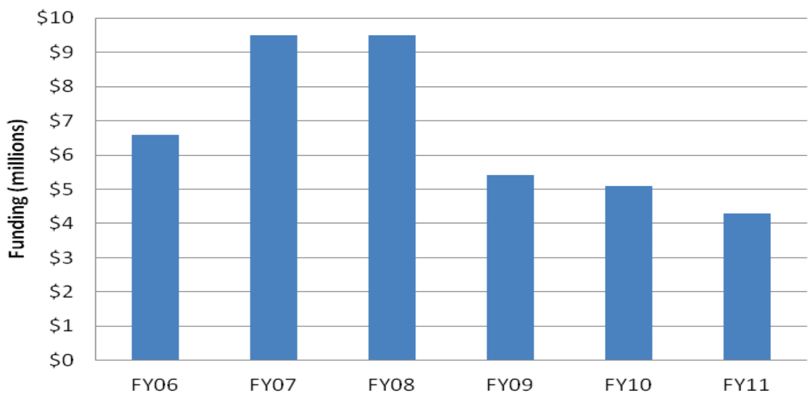

FIGURE C.5-1 Funding of NIH grant awards to researchers in Russia
SOURCE: Information provided by NIH, May 2012.

ship, initially sponsored financially by Eli Lilly and Co., is tasked with organization of annual meetings, conduct of clinical and translational research training courses, and fellowship support for Russian researchers. The first activity was a meeting titled U.S.-Russia Scientific Forum that convened in Moscow in November of 2011. The forum focused on five thematic areas: cancer, healthy lifestyles, human development, infectious diseases, and rare diseases, with more than 200 participants from the United States and Russia. Meetings on brain sciences and cardiovascular diseases took place at the same time in the United States. Ongoing and potential collaborations emerged during the forum, including interest by (a) Duke University and the Institute of Gene Biology to study nanotransporters, (b) several U.S. medical research centers and the Institute of Biomedical Chemistry to study medical proteomics, and (c) the National Institute of Neurological Disorders and Stroke, Washington University, the Institute for Degenerative Disorders, and several institutes of the Russian Academy of Sciences to study preventive treatment of neurodegenerative diseases.

In 2012, NIH and the Russian Foundation for Basic Research agreed to support expanded cooperation on HIV and AIDS. After a competition, 13 projects jointly submitted by Russian and American researchers were approved for funding at an overall level of about $2.25 million. NIH will cover most of the costs of these grants, with the Russian side providing about 10 percent of the total funding. In 2012, NIH also announced a 2-year fellowship program for Russian postdoctoral fellows in biomedical research. The two organizations have also cooperated in carrying out projects in the fields of cancer, autoimmune diseases, neurodegenerative diseases, and Alzheimer disease.

Over the years, NIH has encountered a number of issues in carrying out cooperative programs, including the following:

- Russian taxation of grants to Russian scientists.
- Processing and customs delays and fees on international shipments of biological samples and on equipment transfers.
- Complex grant application procedures.
- Delays in obtaining both Russian and American visas.

SOURCE: Information provided by NIH, September 2012.

Appendix C.6

Centers for Disease Control and Prevention

In the mid-1990s, the Gore-Chernomyrdin Commission facilitated collaborations between U.S. and Russian scientists in a number of fields. The secretary of health and human services played an important role in maintaining an open dialogue concerning mutual interests in public health and medical science. Against this background, the Centers for Disease Control and Prevention (CDC) were among the U.S. agencies to expand collaborative partnerships with Russian scientists.

The expansion of CDC's interests included a new focus on engagement of former Russian defense scientists, with special financing provided through the Defense Threat Reduction Agency (DTRA) and through the Department of State to pursue this expanding interest. An initial effort was directed to activities at the State Research Center of Virology and Biotechnology Vector, in Koltsovo, and the State Research Center for Applied Microbiology in Obolensk.

In the late 1990s, DTRA launched a demonstration project involving five collaborative pilot projects based in Koltsovo and three in Obolensk, at an average cost of $55,000 each. These projects linked U.S. and Russian experts who were experienced in handling especially dangerous pathogens. The initial emphasis was on partnerships involving U.S. government specialists, which led to involvement of CDC personnel.

Building on these early efforts, DTRA financed Russian participation in several follow-on projects, calling on CDC specialists for assistance. However, the sustainability of some projects was questionable because of (a) lack of adequate funding for U.S. participants, (b) limitations of appropriate U.S. investigators' availability to ensure project success, given their other responsibilities, and (c) administrative hurdles that disrupted schedules and led to long delays. Also, on the Russian side there was limited capacity of partner scientists to actively contribute to the collaborations, due in large measure to the poor state of their facilities and the economic crisis disrupting activities at the institutes.

Nevertheless, these initial partnerships helped demonstrate that even under very difficult conditions, it was possible to work together and contribute to scientific progress. Most important, lasting relationships were created. A number of joint research projects eventually evolved in Russia, and CDC personnel continued to play important roles. These projects facilitated transparency and confidence building at a time when serious security issues were paramount.

In the early 2000s, the BioTechnology Engagement Program was developed, with the Department of State transferring funds from its nonproliferation portfolio to several government agencies to support research at Russian institutions, including the Department of Health and Human Services (HHS). HHS in turn arranged for the participation of CDC and other HHS entities in collaborative endeavors. In parallel, DTRA continued to provide funding to CDC for its continued support of DTRA's nonproliferation efforts in Russia, including both research and capacity-building efforts. Also, the U.S. Agency for International Development relied on CDC support as it expanded its health-oriented programs, particularly with regard to AIDS and multidrug-resistant tuberculosis (MDR-TB).

Then in 2008, the Department of State terminated the transfer of its nonproliferation funds to HHS, as the government cut back support for activities in Russia. But a series of disease outbreaks involving Russia led to a continued presence of CDC in Russia and to training of Russian counterparts in Atlanta. Longstanding collaborations on important public health infectious diseases, specifically HIV and MDR-TB (especially within high-risk populations such as prisoners), have remained in place for many years. At least in the case of TB, there have been projects that involved pharmaceutical industry partners such as Eli Lilly.

Also, during the past decade, CDC collaborations have expanded to include a wider range of infectious diseases, with perhaps the most emphasis being placed on influenza surveillance. This focus was stimulated, at least in part, by the Group of Eight (G-8) summit in St. Petersburg in 2006 and global concern regarding possible pandemic avian influenza (influenza A/H5N1). Russia took this opportunity to focus the G-8 health discussion on influenza and to expand Russian programs in influenza.

More recently, collaborations have expanded to a wide range of Russian institutions and a broad set of joint topics. In addition to studies undertaken at the State Research Center of Virology and Biotechnology, Vector, and the State Research Center for Applied Microbiology (four projects), collaborations with CDC principal investigators have involved the (a) Central Institute of Epidemiology (two projects), (b) Engelhardt Institute of Molecular Biology, (c) Gamaleya Institute of Epidemiology and Microbiology, (d) I.I. Mechnikov Moscow Research Institute of Vaccines and Sera, (e) Sechenov Moscow Medical Academy, (f) National Research Institute of Antibiotics, (g) Pokrov Plant of Biopreparations, (h) Research Institute of Phthisiopulmonology, (i) State Research Institute of Biological Instrument-Making, and (j) Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry. At present, CDC has a long-term collaborative arrangement with the Research Institute of Influenza.

Topics that have been undertaken include studies on (a) smallpox, although a genome project on smallpox was approved but not implemented, (b) influenza surveillance, (c) rabies, (d) antimicrobial-resistant *Streptococcus pneumoniae*, (e) beta-lactamase resistance in gram-negative bacteria, (f) improvement of diagnostics for HIV and hepatitis in donor blood, (g) hepatitis C reference panels, (h) investigations of clinical isolates of *M. tuberculosis*, (i) tuberculosis clinical trials, (j) rapid diagnosis of susceptibility testing for *M. tuberculosis*, (k) laboratory determination of resistance to MDR-TB drugs, (l) molecular characterization of rubella virus strains in Russia, (m) rubella epidemiology and surveillance, (n) molecular diagnostics of mixed tick-borne infections (*Ixodes persulcatus* ticks), including tick-borne encephalitis and Lyme disease (borreliosis), Bartonella, and gastroenteritis viruses, and (o) Salmonella surveillance. The total cost to the U.S. government for 19 collaborations in these areas involving 13 Russian institutes has been about $12,200,000. Most of these projects have been successfully completed.

CDC also maintains technical relationships with different counterparts in Russia built around certain categorical disease issues. These involve joint participation in scientific meetings, seminars, and workshops. An example is collaborations on polio eradication. CDC is engaged with Russian partners in several studies on HIV, including mother-to-child transmission, attitudes toward HIV testing, seroprevalence studies, and development of pediatric AIDS guidelines, generally through the Global AIDS Program. Joint efforts also exist on tobacco control.

CDC took the lead in Russia in implementing joint efforts in tobacco control. An Adult Tobacco Survey became the foundation for the efforts of the Ministry of Health and Social Development to develop robust antismoking legislations.

There are occasional information exchanges between public health officials in Russia and CDC dealing with emergent issues, such as outbreaks of foodborne diseases or circulations of influenza strains. This informal dialogue has been in place for many years on a scientist-to-scientist basis, and considerable mutual respect has been engendered through these informal communications. In at least one case, contacts and communications were a direct result of personal friendships made during the early engagement with Vector scientists following the collapse of the Soviet Union.

Plans are in place for joint meetings between U.S. and Russian officials to discuss collaborations in health that will focus on tobacco control, food safety, HIV/AIDS, and TB, with CDC as a primary U.S. partner. However, CDC is primarily a technical agency with expertise in disease detection, surveillance, epidemiology, and laboratory capacity, in addition to public health program implementation; and the involvement of other U.S. agencies seems appropriate. It is not yet clear how such collaboration might progress in the absence of the International Science and Technology Center (ISTC) to facilitate program management and accounting or where funding might originate.

Over the years, the following Russian institutes have been the principal partners of CDC:

State Research Center of Virology and Biotechnology Vector
State Research Center for Applied Microbiology
Central Institute of Epidemiology
Mechnikov Institute of Vaccines and Sera
Research Institute of Influenza

Sustaining advances that have been made will depend upon access to limited funds to allow continued scientist-to-scientist dialogue and technical exchanges coupled with more significant investments in major projects that can be undertaken in true partnership, including shared costs and personnel commitments divided by the two sides. Collaborative projects between CDC and Russian partners have relied on the ISTC to facilitate program management and to handle financial resources. The ISTC consistently played a critical role in this regard and has been part of the basic infrastructure required for the program's success. With changes in management procedures on the U.S. side and the closure of the ISTC in Russia, there are significant hurdles to be overcome in moving resources between countries and distribution and accounting procedures if a similar model of collaboration is to continue in the future.

Of special significance for future activities is the Protocol of Intent between CDC and the Federal Service for Surveillance on Consumer Rights Protection and Human Well-Being to Combat Communicable and Non-Communicable Diseases, signed in 2012 for an indefinite duration.

SOURCE: Information provided by CDC, November 2011 and May 2012, and by committee members.

Appendix C.7

National Science Foundation

The National Science Foundation (NSF) does not typically award grants to institutions or individuals outside the United States, but the foundation does support American researchers conducting work in collaboration with scientists in Russia and in other countries. The majority of Russian-oriented activity is supported through the Polar, Arctic, and Antarctic research programs, although there are examples of Russian-oriented research that is funded by the biology and other programs of NSF. American scientists who are interested in studies involving Russian colleagues or institutions are encouraged to identify counterparts and the nature of their collaborations in their competitive proposals for supporting their own research.

Examples of topics of recent NSF-supported research activities that have included U.S.-Russian collaborative efforts in the biological sciences include the following:

- Protein folding
- Geothermal bacteria
- Phylogenetic analysis of avian species
- Marine data management
- Arctic river plankton
- Synthetic membranes for use to ensure safe drinking water
- Biodiversity in Lake Baikal

NSF has identified a number of benefits from joint U.S.-Russia efforts. They include, for example, the following:

- Availability of a plethora of varied habitats and biomes, as well as species not identified elsewhere in the world, which enhance the scope and quality of inventories and databases.
- Common interests in the biology and ecology of the Arctic region.
- Talented Russian researchers with experience in working with a wide array of microbial species.
- Extensive seed collections unique to Russia.
- Lower costs of research conducted in Russia than of comparable research carried out in the United States.

Challenges for NSF to fund work in Russia include the following:

- Lack of a mechanism to recoup funds or impose penalties for inappropriate use of NSF funds by foreign institutes or researchers.
- Total reliance on individual American scientists to identify appropriate collaborators.
- Competition for limited funds to be used abroad between activities to be carried out in Russia and activities in other regions of high scientific interest (e.g., ecological studies of tropical regions with important biodiversity issues).

SOURCE: Information provided by NSF, December 2011.

Appendix C.8

United States Agency for International Development

The United States Agency for International Development (USAID) has supported many programs in Russia, beginning in 1992. They have included programs in the fields of health, environment, agriculture, and human welfare, as well as in many other areas of relevance to economic and social development.

Among the programs that have been supported at levels of tens of millions of dollars during the past decade have been HIV/AIDS, tuberculosis, reproductive health, maternal and child health, and child welfare programs. Partnerships with the Russian Ministry of Health and Social Development, nongovernmental organizations, and international agencies have provided frameworks for administering the activities and disseminating the results of programs.

Given the vast scope of USAID's involvement in Russia, with cumulative expenditures of more than $2.5 billion, this appendix provides but small snapshots of health-related activities supported in 2003 and in 2010 that provide important examples of the types of work that have been emphasized.

The program in 2003 included the following activities:

- Promoted healthy lifestyles and HIV prevention among the youth.
- Disseminated HIV/AIDS educational materials through a wide array of media outlets.
- Offered technical assistance in support of multidrug-resistant tuberculosis control.
- Supported marketing campaigns for condom use.
- Supported training workshops and conferences, and upgraded laboratory equipment to improve diagnostic capabilities for sexually transmitted diseases.
- Increased accessibility to quality medical care.

- Improved maternal and childhood health programs.

Activities in 2010 included the following:

- Developed model tuberculosis treatment and drug-resistance prevention programs.
- Supported AIDS training and education centers for medical professionals.
- Fostered drug abuse prevention and rehabilitation services.
- Developed standardized approaches to HIV prevention among injection drug users.
- Disseminated HIV prevention education materials to high-risk populations.
- Organized efforts to reduce neonatal mortality.
- Provided teen health and family planning counseling.
- Encouraged best practices in maternal and childhood health.

In mid-2012, plans were under way to significantly reduce the level of USAID's programs in Russia. Only two health-related areas were scheduled for continuation, namely control of tuberculosis and improvement of mother-child health. Activities related to HIV/AIDS had been removed, at least for the immediate future, from further funding consideration.

The Centers for Disease Control and Prevention was to provide the following services to address tuberculosis problems:

- Evaluate methods for diagnosing TB, including the use of rapid tests that are registered and commercially available in Russia.
- Conduct training courses for TB professionals and paramedical personnel.
- Assist in the development of national standards and guidelines for effective TB control, including training curricula.
- Support participation of Russian specialists in international conferences and workshops.

With regard to mother and child health issues, USAID partners were to focus on (a) putting into effect federal guidelines and best international practices and (b) improving the skills, resources, and services at the primary, secondary, and tertiary levels of care. A neonatal resuscitation training course was to be developed in partnership with a Russian center.

As to funding levels, in the late 1990s, USAID programs were funded at levels in the hundreds of millions of dollars annually. During the early 2000s, annual funding levels exceeded $50 million, including more than $10 million to support health-related activities.

Then in September 2012, USAID announced its intention to terminate its

Russia-based activities in response to the request of the Russian government. It was not immediately clear whether programs administered from Washington would continue in Russia, although the U.S. government vowed to stay engaged with Russian organizations with common interests.

SOURCE: Information provided by USAID, Moscow, October 2011 and updated November 2012.

Appendix C.9

Environmental Protection Agency

The Environmental Protection Agency (EPA) has collaborated with Soviet and Russian scientists for 40 years. Since 2000, the Department of State has provided most of the support, with the goal of redirecting former Russian defense-oriented scientists to civilian careers.

Examples of research projects that have reflected fruitful U.S.-Russian collaboration are the following:

- Computational Toxicology. EPA's program goal is to provide fast, automated tests for screening and assessing chemical exposure, hazard, and risk through far broader testing of novel compounds than was previously possible. Collaboration with Russian scientists in the program has proved to be of considerable value.
- Modeling Biological Systems. Projects supported by the International Science and Technology Center have aimed at decreasing uncertainty in chemical risk assessments by incorporating unique models of biological systems in the assessments. Successful collaborations with Russian counterparts have resulted in adoption of new methodology for quantitative analysis of genomics data for use in risk assessment, addressing risks associated with formaldehyde as a case in point. Results have been presented at international conferences and in publications.
- Identification, Characterization, and Functional Assessments of Isolated Wetlands. Through collaboration between EPA and partners at institutes of the Russian Academy of Sciences in Novosibirsk and Krasnoyarsk and at the Siberian Center for Environmental Research and Training in Tomsk, this project has devel-

oped information on the functions of wetlands that are important in improving management of wetlands in both the United States and Siberia.

The joint programs have contributed to advancement of scientific insights. Participants also report benefits in strengthening bilateral governmental ties, improving long-term training of scientists, and bolstering cultural understanding. Areas identified for future research collaboration include environmental endocrine disrupters, environmental mercury contamination, and remediation of nanotechnology releases into the environment.

SOURCE: Information provided by EPA, May 2012.

Appendix C.10

Agricultural Research Service

Beginning in 1998, the Agricultural Research Service (ARS) mounted a cooperative program with scientists in Russia, as well as with scientists in other independent states that emerged after the splintering of the USSR in 1991. The Department of State provided the funding. The International Center for Science and Technology (ISTC) in Moscow conducted onsite administration of projects. The objectives of the program were to (1) advance agricultural science by supporting the development and application of new expertise of Russian scientists, (2) enhance the effectiveness and productivity of ARS research programs that could benefit from extension of activities to Russia, (3) improve the economy of Russia through use of technological advances in Russian agriculture, and (4) reduce the global threat from biological weapons by focusing attention on civilian uses of technologies of concern while ensuring security of dangerous pathogens.

Implementation focused on scientist-to-scientist collaboration with active participation by both sides in jointly designed projects. Projects were funded through grants, usually at a level of about $300,000 over 3 years. Most of the funds were committed to Russian laboratories. ARS limited the funding of its own laboratories to no more than 17 percent of the total funds for any project (commonly, $40,000 over 3 years). This amount could support travel and incidental costs incurred by ARS participants. ARS scientists generally considered such projects to be a part of their personal research programs.

Project selection and approval was a two-step process, driven largely by the ARS collaborators. Brief preliminary proposals developed by either side, which had support by the ARS scientists and concurrence by the ARS national program leader, were considered for support as a direct extension of the ARS program. External peer review was not utilized.

For successful preliminary proposals, the first step was funding of a visit by the cooperating Russian scientists for 1 to 3 weeks to the research facility of the ARS scientist. If the ARS or Russian scientists were not enthusiastic about cooperation after this visit (e.g., a mismatch of capabilities and interests), the process would stop. Otherwise, a full proposal was prepared in ISTC format and reviewed by the governments of the two countries and the ISTC according to ISTC's established procedures.

The ARS review focused, among other things, on compliance with various guidelines, including animal care and use. A requirement for reciprocal yearly visits was included in the proposal. If a proposal was received from a Russian scientist and no U.S. collaborator was named, an effort would be made to locate ARS scientists with relevant skills. Once the proposal was approved, the ISTC then played a key role in providing oversight and resolving problems directly with Russian project participants.

Russian scientists who were struggling financially and who were outside the mainstream of international collaboration enthusiastically greeted the first official visits to their facilities by ARS personnel. It was immediately apparent to the American visitors that the Russian laboratories had well-trained scientists and resources, including pathogen collections that could provide a basis for productive cooperation. The first four projects were approved in 2000 at two Russian laboratories. From 2000 to 2011, about 50 projects were established at Russian laboratories. The program in Russia and other countries that emerged from the USSR has involved more than 30 ARS laboratories and 27 counterpart institutes, with more than 1,300 participating scientists.

Funds expended by ARS through 2011 totaled \$48.2 million, with 45 percent of these funds directed to projects in Russia. Most of the funds were expended in a 7-year period, from 2000 through 2006, when funding available to the ARS for the program totaled \$5–6 million annually. Then funding levels dramatically decreased as the priorities of the Department of State changed.

STRENGTHS AND CHALLENGES TO COOPERATION

Surveys of American scientists involved in the program indicated that the strength of the program was the high quality of scientist-to-scientist interactions that was achieved in almost every case. The principal investigators from both countries contributed to the design of the project, agreed on objectives and procedures, and supported the work throughout the project. Reciprocal visits were considered by most to be not just an adjunct to electronic communications but the true core of the collaboration. In addition, many scientists on both sides reported the building of personal relationships that went well beyond the content of the project.

Of course, there were significant challenges. Movement of biological materials was difficult and was not always sufficiently considered in the development of projects. Some laboratory facilities and vivariums in Russia needed to be upgraded to meet U.S. standards, an issue not always sufficiently considered at the outset. Some Russian laboratories were reluctant to consider cooperation, or such cooperation was discouraged by governing agencies in Russia. Publication of results in international journals was difficult (or a low priority) for some Russian laboratories. This topic deserved discussion at the outset of projects.

There were enthusiastic reviews by almost all participating scientists on both sides. Of the 50 Russian projects, 40 were extended beyond the initial 3-year period, thus providing good evidence of support by collaborators and the authorities from both countries. Many Russian institutes benefited from improved physical facilities and equipment provided through the cooperative projects. However, this statistic does not adequately reflect the strength of the personal relationships formed and the value of such relationships to future research and transparency in science.

Sustainability of projects remains an issue. Few mechanisms for funding of applied projects in agriculture exist in either Russia or the United States. Many promising collaborative projects ended. They could have been continued on a productive basis if financial support had been available. While limited support has been obtained for a few projects, the level of collaboration is unlikely to reach earlier levels.

The original program was considered successful in achieving its objectives, and some aspects of the program can serve as models for future collaborative efforts. At the same time, however, sustainability of research programs in this field is not likely in the absence of a continuing source of government funding.

SOURCE: Information provided by Agricultural Research Service, March 2012.

Appendix C.11

Fish and Wildlife Service

The mission of the Fish and Wildlife Service (FWS) is to "work with others to conserve, protect, and enhance fish, wildlife, plants, and their habitats for the continuing benefit of the American people."

In 1994, the U.S. and Russian governments signed a memorandum of understanding titled "Cooperation in the Field of Protection of the Environment and Natural Resources," which guides bilateral cooperation in this field. The U.S.-Russia border across the Bering Strait makes the two countries pivotal partners for conservation and management of a shared ecosystem. Collaborative efforts have taken the form of information and data exchanges, joint research, disbursement by the FWS of approximately 30 small grants to both Russian and American recipients totaling several hundred thousand dollars annually, and joint management and planning between the (a) FWS and (b) Russian Institute of Ecology and Evolution and Ministry of Natural Resources and Environment.

Activities in 2012 reflect numerous areas of emphasis that developed over the previous 15 years, including:

- Study and conservation of cranes, raptors, marine, and other rare birds.
- Exchange of banding data for migratory birds.
- Study and conservation of polar bears.
- Cooperation of zoos in breeding of species of interest.
- Information and best practice exchanges in wildlife trade and law enforcement.
- Ecosystem biodiversity.
- Management of protected areas.
- Marine mammal conservation and management.

- Plant and animal ecology.
- Aquaculture.
- Arctic ecology and dynamics.

An example of a particularly important activity is the U.S.-Russia Polar Bear Agreement of 2007, which aligns plans for managing a shared population of bears between the countries. It has guided the conservation and management of an iconic species. A joint survey of walrus populations throughout the Bering Strait was also a successful joint effort, with important implications for species management that could not have been carried out without support from both nations.

Lessons learned during the decades of interaction have demonstrated importance of the following approaches:

- Scientific collaboration between specialists who have devoted their careers to similar passions can persist despite political differences between the two countries.
- Small FWS grants to upgrade Russian conservation infrastructure can lead to substantial improvements because of the relatively inexpensive cost of improvements in Russia, particularly when compared to the costs of similar work carried out in the United States.
- Open and regular dialogues between scientists have been more important in maintaining effective collaborative relationships than simply adhering to strictly defined respective roles of scientists from the two countries.

SOURCE: Information provided by Fish and Wildlife Service, April 2012.

Appendix D

Interest of Selected Russian Research Institutions with Active Bioengagement Programs

Appendix D.1

State Research Center of Virology and Biotechnology Vector

The State Research Center of Virology and Biotechnology Vector is one of the largest Russian research and production complexes in the fields of biology and biotechnology. The center's scientific interest is the study of viral infectious pathogens, with the aim of combating diseases and providing biological protection for Russian citizens. Basic research is focused on molecular biology, virology, genetic engineering, biotechnology, epidemiology, and ecology. The assets of Vector include more than 140 highly qualified researchers and engineers with Ph.D. degrees, together with state-of-the-art experimental facilities, including high-containment facilities for the study of dangerous human and animal pathogens.

The International Science and Technology Center (ISTC) research activities in infectious disease research and the potential role of Vector were initially considered during a special seminar at Vector in December 1994. Two research projects—devoted to the development of hepatitis A and measles vaccines—were initiated. Within 2 years, both vaccines were being produced in Russia. However, the success of these initial projects did not lead immediately to further ISTC support, even in an environment of decreased funding throughout Russia for biomedical research during the late 1990s. The U.S. National Academy of Sciences and the Institute of Medicine prepared an important report on bioengagement in 1997 that led to further projects supported by the Defense Threat Reduction Agency of the U.S. Department of Defense. Then, following an international meeting in June 1999 in Stockholm, the Department of State launched the BioTechnology Engagement Program (BTEP), which was very actively supported by the U.S. Department of Health and Human Services, and soon involved Vector.

In 2000, BTEP helped start a few large-scale research projects, including studies of (a) molecular diversity and epidemiology of hepatitis C, (b) epidemiology of hemorrhagic fever with renal syndrome viruses, and (c) smallpox and monkeypox genome sequence diversity. Numerous other cooperative projects in the biomedical sciences were also initiated in Russia, including projects at Vector, with support from various U.S. agencies. A number of projects were devoted to studying the molecular epidemiology of pathogens of public health importance in Russia: viral hepatitis, intestinal infections, influenza virus, tuberculosis, rubella, measles, HIV, herpes, and Crimean-Congo hemorrhagic fever virus. Also, research concerning an HIV vaccine was initiated. Public health projects were later supported by Russian funding agencies as well. Aerobiology of sensitive pathogens was supported and led to the series of well-accepted publications in international journals. Another group of projects was devoted to upgrading biosafety and biosecurity systems by sharing best practices in design, installation, and operation of engineering systems, which were installed and have been successfully maintained at Vector for many years.

International funding allowed for (a) the purchase of materials, reagents, and modern laboratory equipment, (b) disbursement of research grants for individual scientists and teams of scientists, and (c) travel to conferences. The result of these concerted efforts was to bring Russian laboratories up to international standards, while stabilizing the financial situation at Vector and other facilities. In 2002, international funding accounted for more than 25 percent of Vector's budget.

Vector and the State Research Center for Applied Microbiology in Obolensk were initially under the supervision of the Ministry of Health and Social Development, but in 2005 they were moved under the supervision of the Federal Service for Surveillance on Consumer Rights Protection and Human Well-Being. The active engagement of the Federal Service with the two centers provided steady financial support for their research activities.

By 2004, international funding of biosciences projects at Vector had begun to decrease, in part because of (a) policies of the Federal Service and Ministry of Health and (b) U.S. insistence of U.S. agencies that Vector scientists agree not to accept funding from certain foreign organizations that did not support U.S. nonproliferation objectives. Funding from international sources has largely been replaced by increasing Russian government support.

The current world-class scientific research conducted at Vector would not have been possible without the intellectual, financial, and engineering investments from foreign partners, including the ISTC, CRDF, U.S. government agencies, and international organizations.

SOURCE: Multiple sources including Vector and committee members.

Appendix D.2

All-Russian Research Institute of Phytopathology

In the mid-1990s, the All-Russian Research Institute of Phytopathology began collaboration with several large U.S. agro-industrial companies, including Monsanto and Dupont. These companies were interested in officially registered field trials of their pesticides and cultivars (especially with regard to transgenic plants). They entered into contracts with the institute to carry out the required work.

By 2001, the institute had expanded research collaboration with several other U.S. organizations, including the Department of Agriculture, with financial support through the International Science and Technology Center (ISTC). By 2011, 13 ISTC projects had been initiated, with 7 completed. The remaining projects are scheduled for completion by 2013. By 2011, 75 joint articles had been published in international journals, and 1 international patent and 2 Russian patents had been obtained.

Collaborative research projects addressed the following topics:

- Genetic structures of populations of fungal, bacterial, viral, and viroid pathogens that cause economically important diseases in Russia.
- Molecular and genetic testing of the most damaging diseases of cereals and potatoes.
- Creation and maintenance of collections of Russian populations of plant pathogenic microorganisms and nematodes.
- Creation of a genbank of donors and sources of crop resistance to plant pathogens.

- Biologically active molecules of natural origins that are promising for plant protection against phytopathogens (fungi, viruses, viroids, bacteria, nematodes).
- Development of new methods for improvement of forecasts of dangerous phytosanitary situations, using enhanced information technology capabilities.
- Development of nonchemical ecologically acceptable technologies for potato protection against economically significant diseases.
- Genetic adaptation of emerging bacterial plant pathogens of Russia.
- Isolation of novel microbial strains of nematophagous fungi and development and applications of technologies for management of plant parasitic nematodes.
- Search for new extremophilic microbial strains for use as biocontrol agents to improve plant disease management over a wide range of environmental conditions.
- Taxonomic investigations of phytoplasma diseases on potatoes and other crops.
- Development of computer software tools for use in stimulating cereal crop diseases.
- Molecular and genetic characteristics of strains kept within the Russian State Collection of Phytopathogenic Microorganisms.

During the course of these projects, the institute obtained financial support from U.S. partners to obtain modern equipment and reagents for conducting a broad array of investigations. A special unit was established within the Russian State Collection of Phytopathogenic Microorganisms that provides opportunities to work with hazardous pathogens (Biosafety Level 3). Also, a greenhouse equipped with air conditioning and sterilization systems was constructed.

During the early 2000s, biosecurity and biosafety enhancements were introduced into the facilities with U.S. assistance. They provide for consolidation of pathogens in secure storage areas. Also, entry portals into the facilities were upgraded, and improved systems for inventory and control of pathogens were installed.

SOURCE: Research Institute of Phytopathology, May 2012.

Appendix D.3

Research Institute of Influenza

The Research Institute of Influenza in St. Petersburg is one of Russia's leading research centers in the fields of molecular biology, epidemiology, clinical diagnosis of infections, treatment of viral infections, development of sensitive diagnostic reagents, and effective means for public antiviral protection. The institute reports that its principal activities include "exploration of molecular-genetic and phylogenetic features of prevailing and newly emerging viruses, identification of viral genetic determinants, and forecasting of evolutionary variability of influenza and other viral agents."

For more than a decade, the institute has conducted investigations of carbon nanotubes and other nanomaterials. It collaborates with other local research institutions through the Center on Nanomedicine and Nanobiotechnology. This center also coordinates activities of the Ioffe Physical Technical Institute, the Institute of Problems of Mechanical Engineering, and the Bioengineering Center, together with St. Petersburg State Polytechnical University.

Internationally, since 1971 the institute has served as the World Health Organization reference and surveillance laboratory for Russia, drawing on a network of 49 local and regional laboratories across the country. In addition, the institute is interested in markets for diagnostic reagent production, vaccine development, and production of drug-based therapies. In addition, it is interested in chemotherapy drugs, nanovaccines, drug nanocarriers, and antiviral and antibacterial drugs that are based on peptides and recombinant proteins.

Numerous projects have been carried out with U.S. collaborators. The areas of joint interest have included, for example, the following:

- Preclinical trials and testing of broad-spectrum, small-molecule, antiviral compounds, with General Research Laboratories, Inc.
- Investigations of siRNA as a broad-spectrum anti-influenza therapy, with General Research Laboratories, Inc.
- Acute respiratory infection and influenza surveillance and epidemiologist training, with the Centers for Disease Control and Prevention (CDC), including the transfer of 12 Russian influenza strains.
- Development of prototype live-attenuated cold-adapted pandemic influenza vaccines based on avian strains, with the nongovernmental organization PATH Vaccine Solutions.
- Development of a DNA vaccine based on a series of eukaryotic expression plasmids encoding the fusion proteins containing epitopes of influenza, with Cure Laboratory, Inc.

As one current and future example of bioengagement, a joint project with CDC was initiated in 2011, with the intention of continuation until 2016, devoted to the enhancement of influenza surveillance capabilities of the institute. The initial activities have included the following:

- Antigenic and genetic analyses of viruses, which were isolated in Russia, in MDCK cells and chicken embryos.
- Determination of susceptibility of circulating viruses to antivirals, using fluorometric tests and M2 gene sequencing.
- Sentinel surveillance for SARI, to indicate the main groups of risk, determine the most pathogenic circulating influenza viruses, and evaluate vaccine effectiveness.
- Increase in capacity of the institute to identify novel influenza A viruses, with special attention to subtypes H5 and H7 viruses.

SOURCE: Research Institute of Influenza, May 2012.

Appendix D.4

Selected Institutes of the Siberian Branch of the Russian Academy of Sciences

The Siberian Branch of the Russian Academy of Sciences employs more than 8,700 researchers in 74 research institutes and 13 design bureaus. A few bioengagement activities are set forth below. These activities and the future interests of the institutes are less well known in the United States than those of institutes located in Moscow, St. Petersburg, and other cities that are frequently sites of international scientific conferences, as well as being more easily accessible to American colleagues.

INSTITUTE FOR BIOLOGICAL PROBLEMS OF CRYOLITHOZONE, IBPC (YAKUTSK)

IBPC activities are wide ranging. The institute has investigated transcontinental differentiation, ecology, and migration of birds. Researchers have developed technology for mapping areas of locust mass breeding and investigated conjugate evolution of mammals and their parasites in Beringia. Researchers also study dynamics of Asian and European strains of gypsy moth baculovirus and polyhedrosis virus. They participate in monitoring of bird influenza in wild birds in Yakutia. In addition, they have investigated methane emissions from thermokarst lakes.

Collaborative projects have been supported through the International Science and Technology Center (ISTC) and by numerous U.S. partners, including the University of Alaska, Fairbanks; Fish and Wildlife Service; University of Texas; North Prairie Wildlife Research Center; Geological Survey; Burke Museum of the University of Washington, Seattle; Forest Service; Northern Research Station of the University of New Mexico, Albuquerque; and Fairbanks Wildlife Research Center.

The institute is interested in further collaboration in investigating Arctic wildlife.

INSTITUTE OF BIOPHYSICS, IBP (KRASNOYARSK)

In collaboration with the University of North Carolina, IBP developed new nanodiamonds-based materials for medical diagnostics and therapy. Joint projects of the institute and Luminos LLC (Ann Arbor) aimed at development of new bioluminescent probes were supported through CRDF. ISTC supported development of technology of microbial production of the biodegradable polymer Bioplastotan (hydroxybutyrate-hydroxyvalerate copolymer).

The institute is interested in collaboration for further development and production of Bioplastotan-based materials and tools for medicine.

INSTITUTE OF CYTOLOGY AND GENETICS, ICG (NOVOSIBIRSK)

This institute has collaborated with the University of California, Irvine, and the Kavli Institute of Theoretical Physics, Santa Barbara. The National Science Foundation (NSF) has supported bioinformatics research aimed at developing computer-assisted methods for interpretation of biological data and accumulation and systematization of data on gene expression in Arabidopsis. Using original animal models, ICG researchers have performed genetic studies aimed at elucidation of mechanisms of social behavior. This project was developed in collaboration with the University of Utah and supported by the National Institutes of Health (NIH). The institute collaborated with Cornell University's James Baker Institute for Animal Health on investigations of genes responsible for formation of skeletal tissue in mammals. Further collaboration with Georgia State University focused on investigation of human genetic predisposition to severe forms of tick-borne encephalitis. ISTC supported research at Vector aimed at development of oral vaccines against hepatitis B virus, and ICG contributed to this effort.

The institute is interested in further collaboration in several fields: (a) investigation of mechanisms of metastatic tumor growth and development of therapeutics for prevention of metastasis process; (b) computer reconstruction of gene nets describing interaction of viral and bacterial pathogens with mammalian cells; (c) investigation of molecular mechanisms and identification of genes providing resistance of wheat to fungi; (d) identification of molecular targets of different nanoparticles and investigation of molecular, cellular, and physiological mechanisms of response to different nanoparticles; (e) development of micro- and nanofluidic systems for biotechnology and medical diagnostics; and (f) investigation of mechanisms providing reprogramming of somatic cells.

INSTITUTE OF CHEMICAL BIOLOGY AND FUNDAMENTAL MEDICINE, ICBFM (NOVOSIBIRSK)

ISTC and NIH have supported projects at this institute aimed at investigations of (a) mechanisms of DNA repair in mammalian cells, (b) papilloma virus infection and associated epigenetic effects important for progression of cervical cancer, (c) epidemiological studies of tuberculosis in the Novosibirsk region, (d) molecular biology of *Borrelia burgdorferi* (Lyme disease), and (e) ecology of Siberian bogs. CRDF, ISTC, and the Food and Drug Administration have provided grants to ICBFM, along with grants to Vector, for development of oligonucleotide microarrays for identification and genotyping of influenza A, hepatitis C, and orthopoxviruses. Researchers at ICBFM have collaborated with Cornell University on development of computer programs for prediction of biopolymer folding and design of small molecules, targeted to specific nucleic acids and proteins.

The institute is interested in collaboration in the following areas: (a) investigation of infectious agents transmitted by ticks in Russia and the United States on the basis of genetic analysis of pathogens, (b) development of therapeutic phages for controlling bacterial infections, (c) search for viral markers in patients with cardiovascular diseases, (d) investigation of circulating DNA and RNA as potential biomarkers, (e) new approaches for personal and predictive medicine, (e) cell technologies for regenerative medicine, (g) development of telemedicine approaches, (h) development of micro- and nanofluidic analytical systems, (i) investigation of prehistoric and extremophilic microorganisms, and (j) comparative molecular genetic studies of viral intestinal infections.

INSTITUTE OF GENERAL AND EXPERIMENTAL BIOLOGY, IGEB (ULAN-UDE)

The institute is interested in future collaboration in the development of therapeutically useful preparations of medicinal plants.

INSTITUTE OF LIMNOLOGY, LIN (IRKUTSK)

LIN investigated different aspects of ecology of Lake Baikal: microalgae, endemic plants, and fish and animal species. Researchers have isolated biologically active compounds, as potential therapeutics, from endemic organisms. The research was performed in collaboration with a number of U.S. universities (University of California, Davis; University of Washington, Institute of Oceanography, Harbor-Branch; University of Southern Mississippi; New York Museum of Natural History). It has been supported by CRDF, NSF, the Global Change and Climate History Program of the U.S. Geological Survey, the National Geographic Society, and the Samuel Freeman Charitable Trust.

The institute is interested in future investigations of microorganisms and algae populating Lake Baikal.

INSTITUTE OF HUMAN ECOLOGY, IHE (KEMEROVO)

This institute is interested in joint studies for investigating mechanisms of chemical carcinogenesis and development of approaches to prevention and control of harmful processes initiated by chemical carcinogens.

INSTITUTE OF MOLECULAR AND CELLULAR BIOLOGY, IMCB (NOVOSIBIRSK)

Researchers of this institute perform fundamental studies of the organization of animal genomes: *Drosophila* genome was subjected to fine cytogenetic mapping, and comparative phylogenetic studies were performed on mammalians. These studies were supported by NIH. CRDF supported investigations of the epidemiology of inheritable mitochondrial diseases in Siberia and genetic history of ancient inhabitants of Siberia and America.

The institute plans detailed genetic studies of autochthonous Siberians and ancient Americans.

INSTITUTE OF SOIL SCIENCE AND AGROCHEMISTRY, ISSA (NOVOSIBIRSK)

The institute is interested in collaboration in investigations of soil bacteria.

INSTITUTE OF SYSTEMATICS AND ECOLOGY OF ANIMALS, ISEA (NOVOSIBIRSK)

The ISTC, CRDF, and the BioTechnology Engagement Program have supported the following research at this institute: (a) investigations of the epidemiology of influenza virus in wild birds, poultry, and pigs and (b) investigations of genetic and antigenic diversity of hantaviruses circulating in the Asian part of Russia.

The institute plans to develop the following projects in collaboration with American colleagues: development of biological methods for controlling populations of forest pests and insects harmful for agriculture; genetic studies of parasites found in human patients and in Siberian animals; investigation of factors affecting migration of birds in Western Siberia, Kazakhstan, and Middle Asia; and investigation of rare birds of Northern Asia.

SIBERIAN INSTITUTE OF PLANT PHYSIOLOGY AND BIOCHEMISTRY, SIPPB (IRKUTSK)

The ISTC has supported research at this institute aimed at development of transgenic tomatoes as candidates for orally administered vaccines against hepatitis B virus.

The institute is interested in organization of joint studies of Siberian plants and production of transgenic plants for biotechnology applications.

SUKACHEV INSTITUTE OF FORESTRY, IF (KRASNOYARSK)

Researchers of IF have investigated forest structure, health, and sustainability. They have developed methods for fire management in areas of high risk. Also they have investigated effects of fires on carbon cycling. These studies have been performed in collaboration with the University of Arizona with support by NSF and the National Aeronautics and Space Administration. Researchers have investigated pests of the Siberian forests and developed technologies for reforestation of northern territories, with support from the U.S. Forest Service and the U.S. Agency for International Development (USAID).

CENTRAL SIBERIAN BOTANICAL GARDEN, CSBG (NOVOSIBIRSK)

CSBG investigated Siberian plants in the context of the international program of collaboration of botanical gardens supported by the Institute of Sustainable Development and the USAID.

This institute is interested in collaboration on medicinal plants.

SOURCE: Information provided by Siberian Branch of Russian Academy of Sciences, January 2012.

Appendix E

Activities of Other Organizations

Appendix E.1

Bilateral Presidential Commission

President Barack Obama and President Dmitry Medvedev established the Bilateral Presidential Commission (BPC) in July 2009 to identify and support high-priority areas of U.S.-Russian bilateral collaboration. The BPC has worked to broaden and deepen cooperation in many areas of common interest, including health, agriculture, environment, innovation, education, and nonproliferation.

The commission's original Mission Statement is as follows:

> The United States and the Russian Federation reaffirm that the era when our countries viewed each other as enemies is long over. Recognizing our many common national interests, we are resolved to move beyond Cold War mentalities and chart a fresh start in relations between our two countries to contribute to our future progress and shared prosperity. Under the leadership of President Obama and President Medvedev and coordinated by Secretary Clinton and Foreign Minister Lavrov, the U.S.–Russia Bilateral Presidential Commission is dedicated to identifying areas of cooperation and pursuing joint projects and actions that strengthen strategic stability, international security, economic well-being, and development of ties between the Russian and American people. Through the commission's working groups and sub-committees, we will strive to deepen our cooperation in concrete ways and to take further steps to demonstrate joint leadership in addressing new challenges. The foundation for the work of the commission is based on the core principles of friendship, cooperation, openness, and predictability; and we are resolved to address disagreements openly and honestly in a spirit of mutual respect and acknowledgement of each other's perspective.

The Terms of Reference are as follows:

The Bilateral Presidential Commission is intended to serve as a regular and structured mechanism to advance the highest priority bilateral objectives. The coordinators will meet at least once a year. Working groups and sub-committees should be composed of government representatives and shall meet regularly, as often as co-chairs consider necessary.

Guided by objectives set out in the U.S.-Russia Action Plan agreed by the Presidents in July 2009, working group and sub-committee co-chairs should develop an initial list of priority initiatives and a roadmap for moving forward on those initiatives this year. Working groups and sub-committees are encouraged to liaise, where appropriate, with parallel structures from the business community and nongovernmental organizations, and consider their recommendations.

Working groups and sub-committee co-chairs shall report progress, next steps, and unresolved issues to coordinators at least twice a year. Coordinators shall submit overall progress reports to the Presidents at least once a year.

The composition of the commission may change as some objectives are accomplished and new ones are identified. The commission does not preclude or supersede ongoing or future bilateral cooperative efforts that fall outside the commission's structure. Working Group and sub-committee participation should be inclusive and representative of government ministries/agencies that have equities on a particular issue.

As of September 2012, the BPC had created 22 working groups chaired by leaders in each federal government.

SOURCE: Information provided by BPC, January 2012 and August 2012.

Appendix E.2

International Science and Technology Center

The International Science and Technology Center (ISTC) is an intergovernmental organization, created to serve the goals of nonproliferation. It was established in 1992 by the European Union, Japan, the Russian Federation, and the United States on the basis of a multinational agreement and an associated protocol. Norway, Republic of Korea, and Canada have also joined the ISTC as funding parties. The ISTC has been pivotal in coordinating efforts to provide new professional opportunities for former defense scientists from Russia and other countries of the Commonwealth of Independent States, with the aim of integrating them into the world scientific community.

Since its inception, the ISTC has supported a program to (a) engage specialists with defense-oriented experience in civilian scientific work, (b) retain Russian scientific talents, and (c) incorporate previously isolated experts into the international scientific community. During a period of economic unrest in Russia during the 1990s, tens of thousands of scientists found themselves without adequate incomes to support their families, making them potentially attractive targets for nefarious parties with hostile intentions that were in search of technological expertise. The ISTC's nonproliferation objectives have been achieved through project grants that are designed to fulfill research and development (R&D) work for civilian purposes proposed by scientists that possess important advanced technology skills.

Since 1994, the ISTC has provided financial support to more than 900 institutions with about 74,000 project participants. Funds expended for projects have exceeded $860 million for about 2,760 projects.

In the life sciences, 702 projects have been funded, with total expenditures of $234 million (involving about 10,000 bioexperts, including more than 7,000 in Russia).

The Department of State has funded 995 projects via the ISTC in the amount of $221 million, of which 720 were implemented in Russia, with $160 million allocated. Of those projects, 273 have been in the life sciences and funded at a level of $64 million. Total funding for 478 Russian projects in the life sciences (both regular and partner projects) reached more than $180 million.

Permanent sustainability of the ISTC as an organization has not been among the major goals of the program. Rather, efforts have been devoted to funding and implementation of specific projects with explicit technological goals.

With regard to biological-related concerns, special attention has been given to the safety of collections of bacterial and viral pathogens in research institutes. A number of institutes have been involved in the program to upgrade physical security and biosafety systems that was funded by the U.S. Defense Threat Reduction Agency. Fourteen projects were funded for nearly $18 million, beginning in 1999. Also, ISTC projects in the area of medicine and health care were developed following recommendations at international meetings of experts from the World Health Organization (WHO), Centers for Disease Control and Prevention, National Institutes of Health, and Food and Drug Administration.

Russian institute leaders report that ISTC funding was the mechanism that helped institutes not only to survive in the economic duress of the 1990s but also to improve infrastructure, cultivate a community of English-speaking scientific managers, develop leadership, gain recognition in the world community, and engage in world-class research.

Efficacy of funds administered through the ISTC, as determined by expert evaluations, has been higher than funds allocated by Russian organizations because of tax-free and customs-free conditions and transparent management of project funds. International independent audit of projects is a usual ISTC practice.

The ISTC has been able to provide effective informational, scientific, financial, managerial, and procurement services for many institutions. The ISTC developed unique mechanisms of facilitating scientific collaboration, assisting Russians in learning about international standards and regulations and in implementing them in their project practice. The ISTC developed expertise and provided services broadly in technology databases, project management, commercialization of products, competency building, and communication and travel support.

The ISTC partner program enabled private companies, government agencies, and nongovernmental organizations to fund directly R&D projects undertaken by Russian scientists and institutions. Partners working with ISTC-affiliated scientists and institutes could gain access to the established ISTC infrastructure, including in-country project management customs clearance, intellectual property rights support, and searches for R&D needs (matchmaking).

BIOTECHNOLOGY AND ISTC

Biotechnology, including agriculture and medicine, is one of the most active areas of ISTC activity. From 1994 to 2012, about 27.2 percent of all funds were allocated to biotechnology. Table E.2-1 offers examples of biotechnology projects supported by the ISTC, completed in 2011.

The ISTC received a total of 1,359 proposals in the life sciences field during this period. Of those, 702 projects for an amount of $234 million were funded, as displayed in Figure E.2-1.

As presented in Table E.2-2, U.S. governmental partners (Department of Defense, Department of Health and Human Services, Department of Agriculture, Department of Energy IPP, Department of State, Environmental Protection Agency) have funded 207 projects in Russia in the life sciences for approximately $122 million.

The United States funded 146 regular projects in biotechnology for approximately $33 million. Additionally, 127 regular projects in environmental sciences were funded by the United States for $31 million. Table E.2-3 lists areas funded by the Department of State.

The main recipients of U.S.-funded ISTC grants in the Russian Federation in biotechnology were the instiues that were managed previously by "Biopreparat" (Figure E.2-3).

Targeted initiatives are a new approach. Three were developed in biotechnology:

Drug Design and Development—Has been developed to facilitate development of novel therapeutics to combat emerging and reemerging infectious diseases and cancer. The initiative is built upon a set of workshops and projects with a view to establishing long-term, cooperative research and development relationships between research institutes and international health care, pharma, and bioscience bodies.

Probiotics and Health—Was developed to (a) create new platforms for development of alternatives to antibiotics, (b) search for new approaches to develop innovative functional healthy foods on the base of Lactic acid-producing bacteria isolated in Russia, which can be used for prevention and complex therapy of gastrointestinal, urogenital, cardiological, and oncological diseases.

Science and Technology in the Prevention of Biological Threats—Has the objective of developing new techniques and technologies for the rapid detection of a defined list of highly dangerous microorganisms; focusing on the Group of Eight priority of protecting food supplies; and assisting in the development of adequate emergency planning, reporting, first response, and epidemiological analysis.

SOURCE: Information provided by ISTC, April 2012

TABLE E.2.1 ISTC Projects in the Biological Sciences Completed in 2011

Project Title	Russian Institute
Bacteriocin Production and Field Trials for Treating Campylobacter Jejuni and Salmonella spp. in Broilers	State Research Center for Applied Microbiology and Biotechnology, Obolensk
Isolation and Characterization of Novel Antimicrobials Against Staphylococcus Aureus: Bacteriophage Endolysins	State Research Center for Applied Microbiology and Biotechnology, Obolensk
Conservation of Genetic Material and Study of Genomic Structure of Different Variola Virus Strains	State Research Center of Virology and Biotechnology Vector, Novosibirsk
Development and Optimization of Technological Processes for Manufacturing Enzyme Preparations, Including Alpha-Amylase, Glucoamylase, Cellulase, Xylanase, Pectate Lyase, Beta-Galactosidase, Lipase, Phytase	Open Stock Company "Vostok," Kirov
Immunologic and Structural Studies on Mammalian Cell Expressed Recombinant HCV Envelope Proteins E1 and E2	State Research Center of Virology and Biotechnology Vector, Novosibirsk
Carbon Exchange Formation in Boreal Forests of Eurasia	All-Russian Scientific Research Institute of Experimental Physics, Sarov
Development and Demonstration of a Methodology and Software for Risk-Based Land Use Planning and Decision Support	Khlopin Radium Institute, St. Petersburg
Hand-Held Express Detector of Drug Traces Based on a Method of Ion Mobility Increment Spectrometry	Design and Technological Institute of Instrument Engineering for Geophysics and Ecology, Siberian Branch of RAS, Novosibirsk
Development of a Research Center for Tuberculosis Clinical Trials Through the Conduct of a Study of a Modified Treatment Regimen for WHO Category 1 Patients	First Moscow State Medical University/Research Institute of Phthisiopulmonology, Moscow
Phosphorescence Multianalyte Microanalysis of Dried Blood Spots as a Basis of Seroepidemiological Monitoring of Zoonotic Infections Transmitted by Ixodid Ticks	State Research Institute of Biological Instrument-Making, Moscow
Monitoring of Influenza A Viruses in Wild Birds, Poultry and Pigs in the Novosibirsk Region	State Research Center of Virology and Biotechnology Vector, Novosibirsk

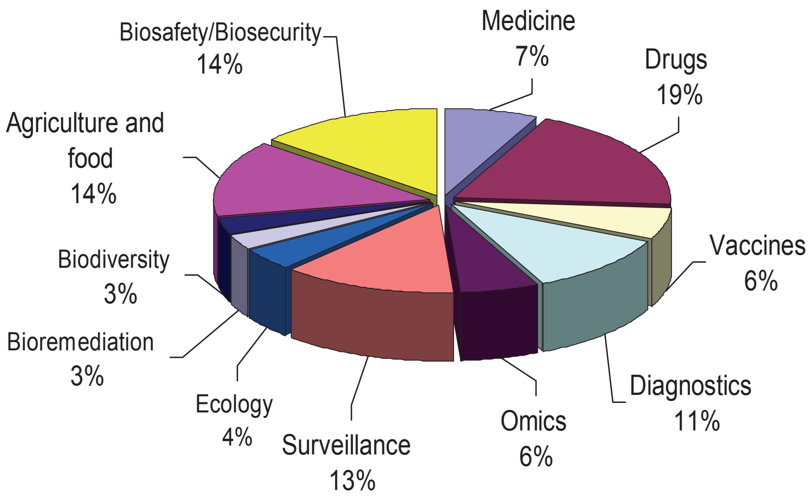

FIGURE E.2-1 Distribution of ISTC-funded biotechnology projects.

TABLE E.2-2 Funding of Biotech Projects in the Russian Federation by U.S. Governmental Partners

U.S. Governmental Partner	Funds, US$	No. of Projects
Department of Defense/DTRA	36,494,286	28
Department of Health & Human Services	30,733,322	59
Department of Agriculture – Agricultural Research Service, Beltsville, MD	23,267,328	50
Department of State – FSU Bio Industry Initiative, Washington, DC	12,488,287	20
Department of Energy / Initiatives for Proliferation Prevention Program, Washington, DC	8,782,500	13
Environmental Protection Agency, Washington, DC	6,803,295	24
Defense Advanced Research Projects Agency, Arlington, VA	3,708,932	13
TOTAL	122,277,950	207

TABLE E.2-3 U.S. Department of State Funding of ISTC Regular Projects in the Russian Federation

Technical Area	Number of Projects	U.S. Allocated Funds, US$	Total Allocated Funds by All ISTC Parties
Agriculture	7	1,431,111.00	1,703,421.00
Biotechnology	73	16,523,441.67	21,060,173.31
Medicine	66	14,766,130.50	17,542,812.22
TOTAL Biotech	**146**	**32,720,683.17**	**40,306,406.53**
Environment	127	31,123,378.00	39,199,622.97
Chemistry	50	13,094,371.34	15,703,197.20
Fission Reactors	65	15,160,771.34	20,935,428.00
Fusion	24	5,070,282.00	8,058,282.00
Information and Communications	27	6,640,754.00	8,666,443.00
Instrumentation	46	10,028,848.58	11,740,661.58
Manufacturing Technology	17	3,795,409.00	4,196,609.00
Materials	61	13,008,816.00	17,297,198.94
Non-Nuclear Energy	23	4,987,150.00	7,946,116.22
Other	4	455,950.00	455,950.00
Other Basic Sciences	1	300,000.00	300,000.00
Physics	104	22,789,612.00	26,270,617.00
Space, Aircraft, and Surface Transportation	22	5,522,976.67	7,798,670.00
Total	**717**	**164,699,002.10**	**208,875,202.44**

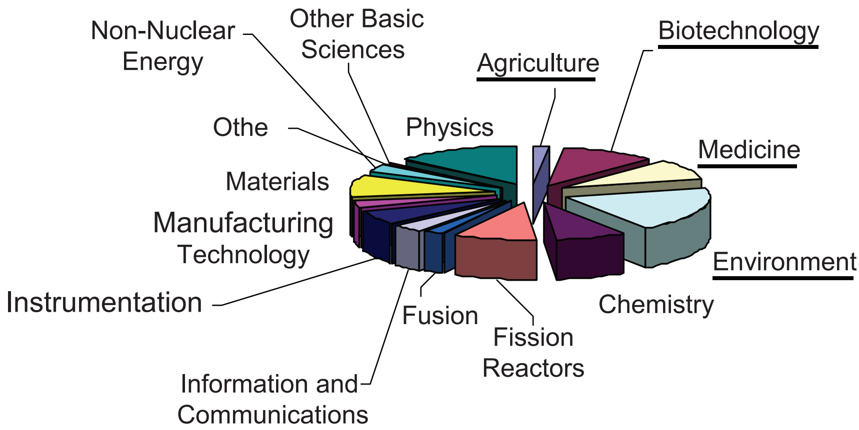

FIGURE E.2-2 Total U.S. funding of ISTC projects. Total Agri+ Bio+Med+ Env = 39%

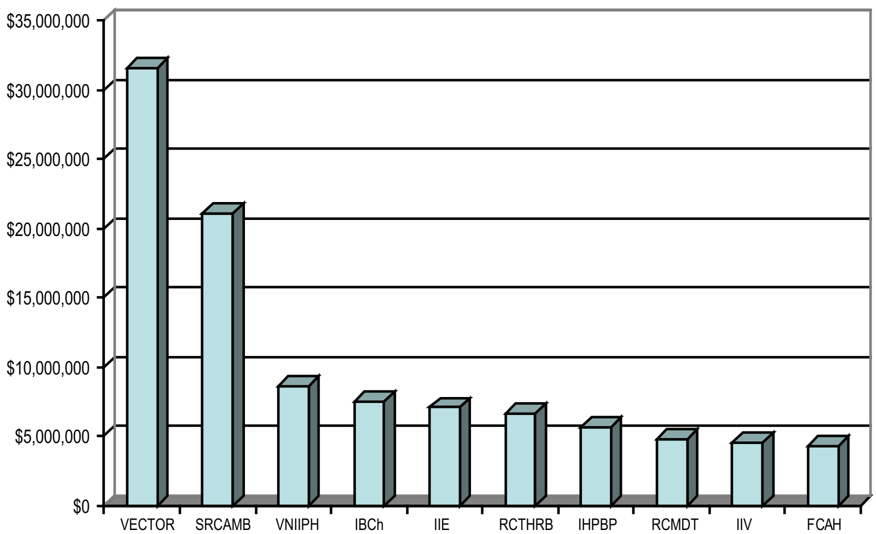

FIGURE E.2-3 Major recipients of ISTC project funds in biology (Vector—State Research Center of Virology, Novosibirsk, SRCAMB—State Research Center of Microbiology and Biotechnology, Obolensk, Shemyakin's Institute of Bioorganic Chemistry, Moscow, Institute of Immunological Engineering, Moscow reg., RCTHRB—Research Center of Toxicology and Hygienic Regulation of Biopreparations Serpukhov, Moscow region, IHPBP—Institute of Highly Pure Biopreparations, St. Petersburg, RCMDT—Research Center of Molecular Diagnostics and Therapy, Moscow, IIV—Ivanovsky Institute of Virology, Moscow, FCAH—Federal Center for Animal Health, Vladimir).

Appendix E.3

Skolkovo Foundation and Innovation Center

The Skolkovo Foundation is a Russian nonprofit organization established in 2010 with the task of creating a science and technology innovation center in the Moscow suburb of Skolkovo. The strategic goal of the Skolkovo Innovation Center is to concentrate international and domestic capital within a hub that will nurture and stimulate the development and commercialization of advanced technologies and house up to 1,000 start-up companies.

The initiative has been financed primarily by the Russian government, which decided to allocate more than $3.2 billion to the activity from 2011 to 2015. The funds are to come largely from the state Bank for Development and Foreign Economic Affairs, Vnesheconombank, with the state's initial commitment fixed at 88.5 billion rubles (ruble-dollar exchange rate in May 2012 was 30-1). The center's budget in 2010 was 3.9 billion rubles. The allocation was 22 billion rubles for 2012 and 17.3 billion rubles for 2013.

The project includes 40 innovation business incubators and technoparks and 80 venture funds—some of which are currently operating in various areas of Russia. In April 2012, there were 1,950 employees at Russian research centers supporting Skolkovo, which are also distributed throughout the country. This number is scheduled to grow to 2,500 by the end of 2012. At this initial stage, there is no requirement for matching contributions for receiving financing from the foundation, but the planned goal is to have 3-1 matching contributions when production activities are initiated. The number of companies that are involved is expected to grow from 20 in 2012 to 30–50 by 2015–2016.

Almost 300 companies/participants have expressed interest in the project. About 20 percent of applications by companies for financial support have been approved. Companies and other organizations with activities under Skolkovo's purview operate by laws that facilitate participation of international companies and encourage innovation. These laws provide tax breaks and administrative benefits, such as onsite customs facilitation and work permit issuance to overcome bureaucratic delays.

Biomedicine is one of the main sectors of interest. Eleven of 30 grant applications for biomedical start-ups had been approved by April 2012. A total of $76 million had been invested, with each grant for $2–5 million over 3–5 years. The strategic goal of the biomedicine cluster is to create an ecosystem for biomedical innovations that consists of more than 90 companies.

The biomedicine cluster focuses on four main fields: (1) clinical medicine and health care, (2) medical-biological and biological sciences, (3) bioinformatics, and (4) industrial biotechnologies (including purification methods and industrial technologies for the production of medical preparations). Plans call for a preclinical medicine testing center for cluster residents that should start operating in 2013. According to this plan, the companies will not have to transfer money from abroad to pay for preclinical testing of medicines.

The following U.S. companies have shown interest in activities of the cluster: Johnson and Johnson, Agenus, Pfizer, AstraZeneca, and Dow Chemical. ChemRar Ventures has entered into licensing and research agreements with Skolkovo Foundation, Johnson and Johnson, and Pfizer.

SOURCE: Information provided by Skolkovo Foundation, April 2012.

Appendix E.4

Skolkovo Institute of Science and Technology

The Skolkovo Foundation, the Skolkovo Institute of Science and Technology (SkTech), and the Massachusetts Institute of Technology (MIT) signed a 3-year contract in November 2011 as an important step in support of education and research activities at the Skolkovo Innovation Center. The goal is to develop a graduate-level research university, together with entrepreneurship programs, at SkTech, bringing together Russian, U.S., and global research capabilities.

The concept calls for 15 multidisciplinary and multi-institutional research centers located abroad, with partners at Russian universities and research institutes as well as at Skolkovo, to work on projects of interest to SkTech. Five are to be located at MIT and 10 at institutions selected on the basis of an international competition. The initial competition attracted 129 applications involving scientists from 360 universities in 20 countries. Each overseas center will be provided with annual operating expenses of $6 to $12 million for up to 5 years. Collaboration is expected to be at the project level, with each center's faculty, researchers, and students collaborating with counterparts from SkTech and one or more other universities within Russia.

Anticipated operation levels are as follows:

- Annual Funding for SkTech after construction: $250 million
- Planned Faculty at SkTech: 200
- Planned Students (masters and doctorates): 1,200
- Planned Postdocs: 300
- Student-faculty ratio: 6 to 1
- Instruction language: English

The expectations are for the faculty to be mostly junior scientists, but full-time and on tenure tracks. Most of the junior faculty will have the opportunity to spend their first year at MIT or another leading university abroad in a faculty development program, including joint research, education development, and innovation mechanisms. The goal is to establish a culture of innovation at SkTech. Industrial advisory groups have been formed to promote ties with industry and public institutions. One of the focus areas is biomedical technologies.

While the Skolkovo complex is private and independent, the initial financial support comes from the Skolkovo Foundation, which receives its budget from the Russian government. Models for the long-term financing will need to be developed, with the goal being a combination of industrial support for the research agendas and operating budgets, including direct funding and endowment support. There is currently no initial endowment, but there is an active development plan for an endowment.

Academic degrees and diplomas will be conferred by SkTech, with certificates issued stating that students have completed a degree program that was developed in cooperation with MIT.

In addition to biomedical technologies, SkTech will focus on the following research topics, which are also the priorities of the Skolkovo Foundation:

- Energy science and technology
- Information science and technology
- Space science and technology
- Nuclear science and technology

The projected near-term timetable is as follows:

2012: First research collaboration centers established at MIT and other locations
2012: Pilot educational programs
2013: Establishment of SkTech

SOURCES: Briefing at Skolkovo Foundation, April 2012; Sarah Everts, "Building an MIT in Moscow," *Chemical and Engineering News*, American Chemical Society, June 25, 2012, p. 40; Briefing by Mats Norlund, Vice President for Research, SkTech, July 2012; "Can Russia Create a New Silicon Valley?" *The Economist*, July 14, 2012, p. 58.

Appendix E.5

Rusnano and Other Russian Investors

Rusnano is a Russian state-owned equity and venture capital fund. It was set up in 2007 as a state-owned corporation with an investment level of $9 billion, but reorganized in 2011 as a joint-stock company. It has a mandate to develop the nanotech industry in Russia by investing in companies in order to develop and commercialize nanotech-based products in Russia with the goal of nanotech sales reaching $40 billion by 2015. As of June 2012, approximately 20 percent of the funds were to be directed to projects in the life sciences.

Investments and commitments by Rusnano and other Russian investors in biotech activities have been announced as follows:

1: Investments in Venture Funds by Russian Organizations:
Venture Fund/ Location/Investor/Fund Value
Domain Associates/U.S./Rusnano (50%)/$760 million
Burrill Capital Fund IV/U.S./Rusnano (40%)/$500 million
Maxwell Biotech/U.S.-Russia/Russian Venture Company/$100 million
RVC Intrafund/Russia/Russian Venture Company/$68 million
RVC Biofund/Russian Venture Company/$50 million

2: Russian Investments in Companies:
Company/Location/Investor/Commitment
ProBonoBil U.K./Russia/Rusnano/$300 million
Nearmedic Plus/Russia/Rusnano/$41 million
Magnisense/France/Rusnano/$38 million
SynBio/Russia/Rusnano/$31 million
Panacela Laboratories/U.S./Rusnano/$26 million

BIND Biosciences/U.S./Rusnano/$25 million
Selecta Biosciences/U.S./Rusnano/$25 million
BIOptics/U.S./Rusnano/$5 million
CardioNova/Russia/Maxwell Biotech/$1–5 million
Hepatera/Russia/Maxwell Biotech/$1–5 million
Infectex/Russia/Maxwell Biotech/$1–5 million
MetaMax/Russia/Maxwell Biotech/$1–5 million

EXAMPLES OF ACTIVITIES OF SPECIAL INTEREST TO RUSNANO:

BIND Biosciences (Cambridge, Mass.): Development in Russia of therapeutic nanoparticles for use in addressing solid tumors, inflammatory, and cardiovascular diseases. http://www.bindbio.com/content/pages/company/aboutrussia.jsp

Selecta Biosciences (Watertown, Mass.): Development in Russia of synthetic vaccine nanoparticles that encapsulate adjuvant and either a T-cell epitope or allergen in a polylactic acid-co-glycolic acid core surrounded by a lipid monolayer and a PEG shell decorated with a B-cell epitope.

Panacela Labs (Buffalo, N.Y.): A 4-year venture between Rusnano ($9 million) and *Cleveland BioLabs* ($3 million) for an oncology subsidiary.

BiOptix Diagnostics (Boulder, Colo.): Development of a surface plasmon-enhanced interferometer-detector for label-free bioassays.

http://cen.acs.org/articles/90/i16/Russian-Investors-Bankroll-biotech.html?h=1167136384. Accessed July 7, 2012.

Appendix F

Other Topics of Interest

Appendix F.1

U.S.-Russian Joint Peer-Reviewed Articles, Reviews, and Conference Proceedings (At least one Russian and one American author) (2000–2012)

Joint U.S.-Russian Publications Identified: 4,392

- Percentage of Joint Russian Publications with U.S. Coauthors: 11.5 percent (U.S. ranks #1 among other participating countries)
- Percentage of Joint U.S. Publications with Russian Coauthors: .36 percent (Russia ranks #25 among other participating countries)

Top Russian Affiliations for 4,392 Publications

- Russian Academy of Sciences: 966
- Moscow State University: 407
- Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry: 218
- Russian Academy of Medical Sciences: 192
- Engelhardt Institute of Molecular Biology: 175

Top U.S. Affiliations for 4,392 Publications

- University of California, Los Angeles: 84
- Harvard Medical School: 83
- Rutgers, the State University of New Jersey: 71
- University of California, Davis: 66
- Indiana University School of Medicine: 64

Top Research Areas of 4,392 Publications

- Biochemistry, Genetics, and Molecular Biology: 2,325
- Medicine: 1,187
- Agricultural and Biological Sciences: 638
- Immunology and Microbiology: 519

Key words for search: bioscience, biotechnology, bioresearch, disease detection, health science, agricultural science, biosecurity, biosafety, toxin, public health, biological weapons, bioterrorism, pharmaceutical, biodiversity ecology, fish, food, environment, animals, crops, antidote, drug.

SOURCE: Scopus Database, October 2012.

Appendix F.2

Russian Research Personnel and Funding

A: TRENDS IN RESEARCH PERSONNEL

Doctorate Degrees Awarded in Selected Fields

	2000	2005	2011
Chemistry	127	94	79
Biology	278	269	207
Agriculture	131	119	79
Medicine	855	793	580
Veterinary	26	43	33

Kandidat Degrees Awarded in Selected Fields

	2000	2005	2011
Chemistry	664	678	767
Biology	1,333	1,462	1,242
Agriculture	354	781	529
Medicine	3,429	4,794	2,854
Pharmacy	86	105	89
Veterinary	199	222	183

Researchers with Advanced Degrees (all fields)

	2000	2005	2010
Doctorate	21,949	23,420	26,789
Kandidat	73,962	76, 018	70,325

Personnel Involved in Research and Development

Total: 839,992	Researchers: 442,071	
State Sector: 33%	Industrial Sector: 48%	Higher Ed. Sector: 19%

B: RUSSIA'S R&D EXPENDITURES

2000	2005	2010
$10.8 billion	$18.1 billion	$32.8 billion

Source of Funds (2010): (For comparison)

	Government	Industry	Other Internal	International
Russia	70%	25%	0.5%	3.5%
U.S.	27%	67%	6%	

Expenditure of Funds (2010): (For comparison)

	Government	Industry	Higher Education	Nonprofit
Russia	31%	61%	8%	
U.S.	10%	73%	13%	4%

SOURCE: Indicators of Science: 2012, Statistical Index, Higher School of Economics, Moscow.

Appendix F.3

Russia's Pharmaceutical and Biotechnolgy Sectors

1. PLAN FOR PHARMA 2020

The plan was set forth by Prime Minister Vladimir Putin, February 2008, to provide a basis for developing the pharmaceutical industry. However, funding began only in 2010. Given the uncertainties in moving forward, the timetable is widely recognized as being overly optimistic; and some anticipated outcomes may not materialize, even after delays. But the program was codified in a government decree in April 2012, and implementation efforts are under way. (Decree of the Chairman of the Government of the Russian Federation, April 24, 2012, No. 1853P-P8, *Complex Program for Development of Biotechnology in the Russian Federation from Now until 2020*)

Objectives by 2020:

- Russian producers' share of domestic market: 50 percent.
- Innovative products in domestic market: 50 percent.
- Average value per product: $40 million.
- Number of innovative molecules: 200.
- Full-cycle production of products within category of "national security": 400.

Milestones:

- By 2012: Import substitution of generics.
- By 2014: 40 licenses for domestic manufacture of Russian products.

- By 2019: Import substitution for 140 drugs and vaccines.
- By 2020: Domestic innovations for 20 exports.

Achieving domestic innovations for export (2016–2020):

- Financing: Grants, venture financing, industry financing. Initial state investment of $1 billion, and eventually industry investment of $1 billion.
- Drugs based on postgenomic period achievements.
- Research centers for drug design.
- New generation of research specialists, together with consultations with foreign scientists.

2. INTERESTS OF RUSSIAN BIOTECHNOLOGY SOCIETY AND BIOINDUSTRY ASSOCIATION

A. ***Regional Biotechnology Programs:*** Tatarstan Republic, Chuvash Republic, Kirov Oblast, Penza Oblast, Karelia Republic, Tomsk Oblast, Novosibirsk Oblast, Kaliningrad Oblast, Belgorod Oblast, Voronezh Oblast.

B. ***Enhancement of Business Structures:*** *Microgen* production of vaccines. *Rosagrobioprom* production of animal drugs. *Bioprocess Group* production of genetically engineered products. *Biotechnology Corporation* development of biofuels. *Biochem Zavod* development and production of animal feed proteins and biofuels.

C. ***Other Initiatives:***

- State program of "Biotechnology Development" (BIO 2020).
- Technology platforms: "Medicine of the Future," "Bioindustry and Bioresources," "Bioenergy."
- Ten new investment projects.
- Skolkovo and Rusnano megaprojects.
- New venture funds.
- Target program of Russian Academy of Sciences, "Fundamental Science for Medicine."
- Increased funding for Federal Target Programs and for Russian Fund for Basic Research.
- Outreach through new journals, Web sites, and conferences.
- Increased educational opportunities for young scientists.

SOURCE: Representatives of Russian Biotechnology Society and Bioindustry Association, September 2011.

3. EXAMPLES OF INVESTMENTS BY COMPANIES REGISTERED IN RUSSIA

- Russian-led joint venture *SynBio* is a $105 million public-private partnership. Rusnano invested $42 million, and the remainder was by Russian-owned HSCI, Russian-owned *Pharmasynthez*, U.K.-owned Lipoxen, and German-owned SymbioTec. The owners invested cash, stock, and intellectual property. First products include (a) drugs based on Histone H1 for cancer and other diseases, and (b) Poplyxen for biobetters aimed at diabetes mellitus, Alzheimer disease, chronic kidney disease, and cardiovascular disorders.
- *BIND Biosciences*, with an investment by Rusnano of $25 million, is to develop new therapeutics against cancer, inflammatory diseases, and cardiovascular disorders. Rusnano has also invested $25 million in *Selecta Biosciences*, which is developing synthetically engineered vaccines for smoking cessation, type 1 diabetes, cancer, and allergies. Both companies were cofounded by professors at Harvard Medical School.
- Another Rusnano-funded company at $4.5 million, *BiOptix Diagnostics*, is a maker of label-free biodetectors.
- Also, Rusnano invested $26 million in *Panacela Labs*, a subsidiary of Cleveland BioLabs.

SOURCE: www.genengnews.com/keywordsand tools/print/3/25235/; accessed March 10, 2012.

4. EXAMPLES OF OTHER INVESTMENTS BY INTERNATIONAL COMPANIES

- Viiv, a venture of GlaxoSmithKline and Pfizer, agreed to supply bulk products, technology, and expertise to the Russian firm *Binnopharm*, which will carry out secondary manufacturing and packaging of drugs for HIV treatments.
- *Roche* granted *TeaRx* development and commercialization rights for treatment of patients in Russia at risk of thrombosis. TeaRx is scheduled to launch clinical studies in 2012 in Russia. TeaRx may add additional drugs to its portfolio.
- *ChemRar* and Pfizer have announced a collaboration focused on drugs and vaccines for cardiometabolic infection and oncological diseases.
- *Johnson and Johnson* signed a Memorandum of Understanding with ChemRar in June 2012 to launch a number of initiatives within the next 5 years for the treatment of tuberculosis, cancer, and hepatitis C.

5. DEVELOPMENT OF RUSSIAN BIOTECHNOLOGY PLATFORMS FOR NEW PRODUCT DEVELOPMENT

- Platform participants assessing inputs from state representatives and experts in a wide array of fields, including:
    - Forest biotechnology
    - Food biotechnology
    - Aquaculture biotechnology
    - Industrial biotechnology
    - Agricultural biotechnology
    - Ecobiotechnology
- Participating institutes include:
    - Siberian State Medical University
    - Lomonosov Moscow State University
    - Russian Technologies State Corporation
    - Kurchatov Institute for Atomic Energy
- Specific priority areas for the near future include:
    - Biorefineries
    - Platform chemicals
    - Bioplastics and biomaterials
    - Biocatalysis
    - Transgenic plants and animals
    - Valorization of waste
    - Pulp and paper
    - Functional foods and feeds

SOURCE: Russian Biotechnology Association, September 2011. Updated during subsequent discussions in Moscow.

Appendix F.4

Assessment of Developments in Agrobiotechnology in the United States and Russia

[Summarized Version]

Dr. Peter Raven and Dr. Konstantin Skryabin[1]

September 2011

INTRODUCTION

Genetically engineered (GE) crops were first commercialized in 1994 in the United States. In 2010, 148 million hectares in 29 countries, or 10 percent of the world's agricultural land, were planted with GE crops (1). They have not yet been commercialized on more than a pilot scale in Russia.

Current GE technology has the capability to protect crop yields, improve water and soil quality, and improve feed grain safety (2). Future innovations in this field may increase efficiency in the use of water, sunlight, and fertilizer; increase tolerance to drought, frost, and salinity; improve photosynthesis; and make the crop's use of nitrogen more efficient. GE traits can directly improve the nutritional qualities of the foods produced as well: high vitamin or protein levels, fruits with delayed ripening, and oilseeds with lower saturated fat. GE crops can also be designed to produce pharmaceutical compounds for human and animal health.

[1] This assessment was prepared in accordance with a joint decision of the Russian Academy of Sciences and the National Academy of Sciences in June 2009 to have experts prepare an analysis of the safety aspects of the introduction of genetically engineered organisms into agricultural systems. The authors express their appreciation to the staff of the National Academy of Sciences and to the members and staff of the Russian Academy of Sciences who supported this activity.

INTERNATIONAL PRINCIPLES GUIDING THE REGULATION OF GE ORGANISMS

In 2003, the Codex Alimentarius Commission, a joint body of the Food and Agriculture Organization and World Health Organization, issued *Principles for the Risk Analysis of Food Derived from Modern Biotechnology* (3). Building on the concept of *substantial equivalence*, the *Principles* instruct regulators to assess GE food products for toxicity, allergenicity, stability of the inserted gene, and nutritional or other unintended effects resulting from gene insertion. The regulatory system in the United States follows these principles. However, parties to the Organization for Economic Cooperation and Development have expressed different degrees of comfort with the concept of substantial equivalence (4). Governments agree to the need for appropriate risk assessment, but nations disagree as to the level of risk that should be accepted in applications of this technology.

In the world's experience of 15 years of commercial use of GE crops, analysis of the results of specialized studies, national data (5), and international scientific assessments, there has not been a single proven case of toxic or adverse effects of GE crops that have been registered as food or feed. In addition, there are no scientifically credible reports indicating adverse ecological effects of commercialized biotech crops.

AGRICULTURAL BIOTECHNOLOGY IN RUSSIA

The development of a national regulatory system for GE in Russia began in 1995–1996. The law FZ-86 (amended in 2000 and 2010) has been the main legal tool for the protection of the environment and human health and for governing relations arising within the conduct of GE activity. More than 60 laws, regulations, and other regulatory documents supplement the legislation for safe use and environmental release of GE crops (6). Unfortunately, they are sometimes not coordinated with one another. A distinctive feature of the Russian registration system is its three separate streams: (1) safety assessment for environmental release from GE crops, (2) safety assessment of GE food, and (3) safety assessment of GE feed.

During 1999–2011, 20 GE lines developed by Russian scientists passed the full cycle of medical and biological studies. Currently, 17 GE lines are approved for use in food (four soybean lines, nine maize lines, two potato varieties, one rice line, and one sugar beet line).

The technical capability is certainly present in Russia to allow the development of agriculturally important products. For example, in 2010, the Russian Academy of Sciences developed fast-growing transgenic aspen and Lombardy poplar as potential sources of biofuels. Russia could play an important role in bioenergy, a commercially attractive industry, by producing fast-growing plants, including GE willow, poplar, and miscanthus.

However, a serious concern is a "de facto moratorium" on seed production and large-scale cultivation of GE crops in the open systems in Russia, which has existed since 2004. In 2002, the Ministry of Industry and Science gave preliminary approval to the registration of two GE potato varieties resistant to the Colorado potato beetle (Superior NewLeaf and Russet Burbank NewLeaf of the Monsanto company), but the registration process was discontinued. As a result, not one square meter of land in Russia is used for growing GE crops, a condition that continues lower productivity, lower value of the crops, more use of chemical pesticides and fertilizers (which sometimes pose problems to the health of humans and animals), and more energy used on crops, with a concomitant increase in the production of greenhouse gases.

AGRICULTURAL BIOTECHNOLOGY IN THE UNITED STATES

In order for a GE crop to be approved for commercial use in the United States, it must pass through the regulatory review process to ensure it does not have unforeseen adverse effects on food safety or the environment. Soybean, corn, and cotton have been the most successful GE crops commercially, and about one-half of U.S. agricultural fields were planted with a GE variety of one of these crops in 2010. GE varieties of canola, sugar beet, papaya, squash, sweet corn, potato, and alfalfa have also been commercialized; however, GE potato and tomato are no longer sold.

Intellectual property law in the United States grants seed innovators exclusive rights to multiply and market new varieties, including those developed with GE technology. These proprietary rights give companies control over the seeds even after they have been purchased by farmers. Research, development, and commercialization is an expensive and time-consuming endeavor, so it is not surprising that the private sector has focused its efforts on soybean, corn, and cotton, which are likely to generate returns on investment because of their dominance in U.S. agriculture. Conversely, public research has addressed issues in much smaller markets. For example, commercialization of GE papaya, which in the United States is only grown in Hawaii, was undertaken by the public sector to prevent a virus from devastating papaya production.

GE technology has not been introduced into a wider array of crops, because few other crops are planted on so many acres. Introducing GE traits into less widely grown crops increases the regulatory costs as a percentage of the costs invested in research and development. Also, the environmental risk associated with gene flow from GE plants to non-GE plants is lower for corn, soybean, and cotton than for most other crops.

Resistance by consumers and growers has been a barrier to further commercialization of the technology. Consumers appear to be more willing to accept GE products that are further removed from direct human consumption. Corn and soybean are used primarily for animal feed and are often highly processed when in food products. It is estimated that 70 percent of all processed U.S. food contains products from plants that have GE characteristics. However, products from crops that are consumed directly by humans, such as wheat, rice, and potatoes, seem to cause more concern. Some U.S. wheat growers have been wary of the commercialization of GE wheat for fear that Japan could issue an import ban on all wheat if the United States grew any GE varieties, although there are signs that this reluctance is weakening as the need to enhance wheat production worldwide becomes more evident.

There have been instances when unapproved GE crops have entered the U.S. food system. When this has occurred, the U.S. government has addressed the issue quickly and determined that the inadvertent releases did not present a health or environmental risk. The U.S. regulatory system has proved effective in ensuring the safety of GE food for consumers and managing GE crops in the environment.

RECOMMENDATIONS FOR NEXT STEPS

If GE crops were to have a level of absolute safety far beyond that required for competitive crop varieties before being used, they would never be used. But as has been demonstrated in many countries, a reasonable level of safety can be ensured through sound regulatory practices. The U.S. and Russian academies of science could work together to improve understanding of the need for safety evaluations and realistic expectations from these evaluations.

The authors of this paper suggest that the following steps be undertaken by the academies in the two countries:

- Letters to appropriate officials of the two governments calling for reexamination of the characterization of risks related to GE crops, taking into account recent advances in GE approaches and the available evidence as to the risks associated with GE crops that are currently being produced.
- Holding of an international forum on scientific opportunities and regulatory barriers concerning the future contribution of GE crops to the global food supply, perhaps organized by the InterAcademy Council.
- Development of a communications strategy for improving understanding of both governments and the public on issues related to GE crops, including food safety, coexistence with organic and conventional crops, ecological benefits, and other aspects of GE crops.
- Encouragement of educational programs in genetic engineering, bioethics, and modeling of scenarios for implementation of innovations in GE technology, with participation of students and young researchers.

Finally, we recommend that approaches to ensuring appropriate food and environmental safety of GE plants and animals should be on the agenda of the

InterAcademy Council, for consideration by experts from countries throughout the world with their recommendations sent to the appropriate bodies of the United Nations, to relevant international scientific organizations, and to interested regional organizations.

REFERENCES

1. James, C., *Global Status of Commercialized Biotech/GM Crops,* ISAAA Brief 42-2010: Executive Summary, The International Service for the Acquisition of Agri-biotech Applications, 2011.
2. National Research Council, *The Impact of Genetically Engineered Crops on Farm Sustainability in the United States*, Washington, D.C., National Academies Press, 2010.
3. CAC (Codex Alimentarius Commission), Principles for the Risk Analysis of Food Derived from Modern Biotechnology, CAC/GL 44-2003, Food and Agriculture Organization/World Health Organization, Rome, 2003.
4. OECD (Organization for Economic Cooperation and Development), Science*, Safety and Society*, Conference on new biotechnology food and crops, Bangkok, July 10–12, 2001.
5. "A Decade of EU-funded GMO Research (2001–2010)," http://ec.europa.eu/research/quality-of-life/gmo/index.html, Skryabin, Konstantin, editor, *Agrobiotechnology in Russia and in the World*, Bioengineering, Russian Academy of Sciences, 2008.
6. Russian Federal Laws, "On State Regulation of Genetic Engineering Activity" (FZ-86, 1996, amended in 2000 and 2010); "On Sanitary and Epidemiological Well-being of the Population" (FZ-52, March 30, 1999); "On the Quality and Safety of Food Products" (FZ-29, January 2, 2000); "On Amendments to the Federal Law 'On Protection of Consumer Rights'" (FZ-234, October 25, 2007); "On Environmental Protection" (FZ-7, 2002).

Appendix F.5

Scientific Forum for Biomedical and Behavioral Research

Results are presented below of a November 2011 meeting in Moscow, organized under the auspices of the Foundation for the National Institutes of Health, to foster U.S.-Russia scientist-to-scientist collaboration and to organize training courses for Russian scientists.

A: THEMATIC AREAS OF INTEREST

Active and healthy lifestyles
Brain sciences
Cancer
Human development
Cardiovascular disease
Infectious and rare disease
Clinical and translational research training

B: PARTICIPATING COMPANIES

Eli Lilly, Amway, Amgen, Abbott, Coca Cola, Johnson and Johnson, Genzyme, Pfizer, Pepsi Cola, Bristol Myers Squibb, Bach Pharma, Celgene, Merck, Genetic Alliance, Novartis, ChemDiv, and ChemRar.

C: ONGOING AND PROPOSED PROJECTS

1: Conjugated Vaccine against *Pseudomonas aeruginosa*

- Interested Russian organizations: Zelinsky Institute of Organic Chemistry, High Chemical College, Mechnikov Institute of Vaccines and Sera, Federal State Unitary Company Microgen Scientific Industrial Company for Immunobiological Medicines
- Interested U.S. organization: Harvard Medical School

2: Simultaneous Multitarget Therapy of Tumors

- Interested Russian organizations: Institute of Chemical Biology and Fundamental Medicine, Vavilov Institute of General Genetics, Institute of Gene Biology, Institute of Molecular Genetics, Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Blokhin Cancer Center

3: Modular Nanotransporters and Chemically Synthesized Modules

- Interested Russian organization: Institute of Gene Biology
- Interested U.S. organization: Duke University

4: HIV-Tuberculosis Diagnosis and Drug Discovery

- Interested Russian organizations: Ivanovsky Institute of Virology, Central Research Institute of Tuberculosis, Central Research Institute of Epidemiology, Vavilov Institute of General Genetics; Institute of Organic Synthesis; Institute of Organic Chemistry
- Interested U.S. partners: Ely Lilly, Infectious Disease Research Institute of Seattle

5: Medical Proteomics in the Context of Bioinformatics Strategy DELSA (Data-Enabled Life Sciences)

- Interested Russian organization: Institute of Biomedical Chemistry
- Interested U.S. organizations: Houston Children's Hospital, Fred Hutchinson Cancer Research Center, Center for Computational Medicine and Biology at the University of Michigan, Department of Chemistry and Chemical Biology at Northeastern University

6: Human Microbiome: Metagenomics, New Biomarkers of Disease, Translational Research in Personalized Medicine

- Interested Russian organizations: Vavilov Institute of General Genetics, Institute of Chemical Biology and Fundamental Medicine (Novosibirsk), Institute of Biomedical Problems, Moscow State University, Research Institute of Physical-Chemical Medicine
- Interested U.S. organizations: Institute for Genome Sciences, University of Maryland School of Medicine, George Mason University

7: Preclinical Development and Preventive Treatment of Neurodegenerative Disease

- Interested Russian organizations: Institute of Developmental Biology, Institute of Molecular Genetics, Institute of Bioorganic Chemistry, Institute of Physiologically Active Substances, Institute of Evolutionary Physiology and Biochemistry (St. Petersburg), Institute of Normal Physiology, Zakusov Institute of Pharmacology, Moscow State Medical University
- Interested U.S. organizations: National Institute of Neurological Disorders and Stroke, Washington University, Institute for Degenerative Disorders

D: PROPOSED FORUM MEETINGS

2012: Rare Diseases and Drug Development
2013: Brain Sciences
2014: Infectious Diseases and Cancer
2015: Healthy Lifestyles and Cardiovascular Diseases

E. POTENTIAL FUNDING ORGANIZATIONS IN RUSSIA

Ministry of Education and Science, Ministry of Industry and Trade, Skolkovo Foundation

SOURCE: Ann Ashby, NIH Foundation (Ann.Ashby@NIH.gov).

Appendix F.6

Funding and Related Mechanisms

(Examples of established or new mechanisms of relevance to proposed Research Fund)

1: International transfers of money, equipment, and materials

- Deposit of funds provided by institution in one country in bank account of recipient institution in other country.
- Transfer of funds provided by institution in one country directly to recipient scientist in other country—transfer into bank account, by personal delivery of cash or check, or by payment of personal expenses (airfare, hotel, etc.).
- International transfer of funds via CRDF.
- International transfer of funds to institution or individual through commercial service-provider—travel agency, overseas affiliate of paying organization, or multinational service-provider.
- Payment to producer or commercial handler of material and equipment in one country for purchase and shipment abroad to user of material and equipment, including payment of customs fees.

2: Organizations with relevant experience in awarding international research grants and contracts in the life sciences on a competitive basis

- U.S. government organizations: Department of State, National Science Foundation, National Institutes of Health (NIH), Centers for Disease Control and Prevention.
- U.S. nongovernment organizations: CRDF, Howard Hughes Medical Institute, NIH Foundation.
- Russian ministries and agencies: Department of Education and Science; Ministry of Health and Social Services.

- Other Russian organizations: Russian Foundation for Basic Research (RFBR), Skolkovo Foundation, Rusnano.

3: Other relevant experience

- Parallel awards in two countries by government and/or nongovernment entities for joint projects (e.g., NIH-RFBR; Russian Department of Education and Science-U.S. Department of Education).
- Fund transfers within Joint Ventures.
- U.S. government guarantee of repayment of Bank Loan to support commercially oriented project in Russia.
- Fulbright program to support researchers from one country carrying out exploratory or well-defined research in other country.

4: New models

- Expanded role of existing foundation (e.g., Bill and Melinda Gates Foundation, U.S.-Russian Foundation for Economic Advancement and Rule of Law, Rostropovich Foundation).
- Establishment of new fund within appropriate existing organization (with or without endowment) that has experience in funding international projects in the life sciences.
- Location of funding organization or recipient organization (or both) within special tax and customs zone.