International Collaboration Is the Basis for Infectious Disease Control and Combating Bioterrorism
*The G8 Global Partnership Against The Spread Of Weapons and Materials of Mass Destruction*
*23-24 April 2004, Moscow*

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I represent the State Research Center of Virology and Biotechnology VECTOR that is an institution of the Russian Ministry of Health. Before 1991, VECTOR was involved in biodefense research. I would like to briefly tell you about our institution. Today, the State Research Center of Virology and Biotechnology VECTOR is one of Russia's largest scientific research and production facilities whose major activities are focused on carrying out basic and applied research in a wide area of natural sciences, development and manufacture of therapeutic, preventive, and diagnostic products for public health and agriculture and for combating bioterrorism.

In my presentation I would like to address the need for international cooperation on combating bioterrorism. During the recent decade, policy makers, military and civilian experts have shown more and more interest in the bioterrorism issue. Possible biological agents of viral or bacterial etiology, scenarios of how to prevent from and respond to the use of these agents, and epidemic response capabilities in terms of the availability of competent personnel, diagnostic and therapeutic products have been discussed and analyzed.

As a rule, the scenarios of bioterrorism incidents are far from being optimistic in terms of both human casualties and costs associated with containing direct consequences of such actions as well as with an economic breakdown in the region affected and lasting psychological effect they produce on the population [1, 2].

Terrorism now is a growth industry and the possibility of a chemical or bioterrorism attack is increasingly defined as “not if, but when”. I should especially emphasize important features that make bioterrorism different from other kinds of terrorism [3, 4].

Explosive substances are pretty widespread and not that diverse. Chemical agents that could be used for terrorist purposes are well-studied as potential chemical weapons agents and for many of them detection procedures as well as treatment of those affected and decontamination have been developed. In case of biological agents, it is an absolutely different situation. However, the study of the effect of chemical and radiological factors on the pathogenesis of infectious diseases and investigation into how properties of infectious agents are influenced by these factors appears of enormous importance.

In nature, there are a great variety of viruses, bacteria, and fungi causing diseases in humans, animals or plants. Nature is continuously creating new pathogens, the so-called “emerging infections”, and this potential is just inexhaustible. The most recent example of this is the SARS situation, a disease known as Severe Acute Respiratory Syndrome as well as the avian influenza H5N1 situation. During the last 25 years alone, over 30 new infectious agents e.g. HIV, Marburg, Ebola, Machupo, Nipah virus and SARS-associated coronavirus have been discovered against which no efficient treatments are available so far.

An outbreak of disease elsewhere on the globe can now be viewed as a threat to any other region of the world. Once an infectious disease, or the insects and animals that carry it, invades a new country or continent, it can prove difficult – if not impossible – to control.

Known diseases such as influenza, TB, malaria and some others, through their changeability, can relatively easily overcome conventional immunization and drug-based approaches to prevention and therapy.

Though biological weapons-and bioterrorism experts often operate with a limited list of several dozens of infectious agents on it, we should not underestimate the possible terrorist use of any of diverse pathogens existing in nature.

So the task of establishing a global system of surveillance of possible natural or artificial outbreaks is far more difficult than that of chemical agents or explosives.

It is important to realize that biological agents act in time, have a latent period during which the carrier of infection may find herself/himself in another city or even country, where the outbreak of disease may be actually identified, and it may take much time to prove the bioterrorist use of microorganisms since it will require a comprehensive epidemiological analysis, e.g. investigation of all the stages of manufacture and distribution of food-stuffs in case of food poisoning.

A qualitatively more difficult problem is that of keeping the inventory of the pathogens during research work since during such activities the biological agents, as a rule, grow in quantity and can be represented by not

only individual pathogens but also by being present in experiment in the form of infected cell cultures, laboratory animals etc. Insignificant, hardly accountable quantities of a biological agent, may pose a real threat in terms of uncontrolled leakage of biological material. Unfortunately, this problem does not yet have either an engineering or technical solution. In fact, it is determined by the human factor, i.e. it is necessary to adopt criteria and requirements to personnel to be allowed to work with pathogens, even within the highly secured laboratory facilities.

An associated problem is that highly pathogenic agents are many and they might be accessed during natural outbreaks of disease. Moreover, they can be engineered through simple laboratory manipulations on the non-pathogenic microorganisms available.

Therefore, it is medical staff that turn out to be the first to have to deal with biological incidents and it is the public health capabilities that determine the preparedness of a country, region or city for a timely detection and elimination of consequences of the use of biological agents. Therefore, financial and organizational efforts should be focused on civilian rather than military agencies.

The nation must be prepared to deal with detection and elimination of consequences of outbreaks caused by any biological agents, including both conventional and exotic species of microorganisms. The existing national systems of nation-wide epidemiological surveillance and control of infectious diseases should be capable of identifying, containing and eliminating an infectious disease outbreak regardless of whether it is the result of natural manifestation of a pathogen or its deliberate use.

I should point out these features of control over biological agents and say that that international collaboration in this area is both extremely important and urgent in order to set up a system of efficient alert and response. This issue was specifically addressed in May 2001 during the 54th World Health Assembly in the report by the Secretariat "Global Health Security - Epidemic Alert and Response" (http://www.who.int/gb/EB_WHA/PDF/WHA54/ea54r14.pdf).

The WHO Secretariat pointed out the increased possibility of intentional use of agents causing infectious diseases and emphasized that natural epidemics and those due to the deliberate use of biological agents may manifest themselves in the same manner.

In 1997, WHO established a special system to seek, collect and verify information on reported outbreaks based on close cooperation of WHO Collaborating Centers with governmental and nongovernmental agencies, which is available as confirmed disease outbreak news on the WHO web site (www.who.int/disease-outbreak-news/) and in the WHO Weekly Epidemiological Record (www.who.int/wer). At global level, laboratory networking takes place (http://www.who.int/csr/en/), focusing on such infections as hemorrhagic fevers (including Ebola virus), poliovirus; preparation of databases such as the WHO antimicrobial resistance data bank (ARInfoBank) (www.who.int/emc/amr.html), influenza FluNet (http://oms2.b3e.jussieu.fr/flunet/), rabies RabNet (www.who.int/emc/diseases/zoo/rabies.html), and some others. WHO also called the member states to establish partnerships to involve both civilian public health and military medical capabilities.

WHO continuously draws the attention of its member states to the ultimate role of national potential to ensure epidemiological welfare of other countries and so it plans to expand national training programs in intervention epidemiology worldwide, and the Training in Epidemiology and Public Health Interventions Network (TEPHINET). Major conclusions based on discussions of the Secretariat Report were reflected in resolution WHA54.14 "Global Health Security: Epidemic Alert and Response" (http://www.who.int/gb/EB_WHA/PDF/WHA54/ea54r14.pdf).

To detect and counteract bioterrorism, the National Institute of Allergy and Infectious Diseases (NIAID/NIH) has developed a biodefense research agenda for CDC A Category Pathogens such as smallpox, plague, tularemia, anthrax, botulinum toxin, etc. (http://www.niaid.nih.gov/biodefense/research/biotresearchagenda.pdf). As part of this strategic plan, the NIAID is establishing the Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research (RCE) Program and Biocontainment Laboratories (BL) (http://www.niaid.nih.gov/biodefense/rblrce.htm). The RCEs and BLs will contribute to the need for new infrastructure and research resources necessary for identifying and responding to emerging diseases and bioterrorism events.

A Global Partnership, launched by the G8 leaders at the summit at Kananaskis in Canada in June 2002 appears to be a qualitatively new stage of international collaboration on nonproliferation and countering bioterrorism (http://www.sgpproject.org/jointstatement.html; http://www.csis.org/pubs/2003_protecting1.pdf). It seeks to achieve the following goals:

- promote multilateral treaties that help prevent the spread of weapons, materials and know-how;
- account for and secure these items;
- promote physical protection of facilities;
- help detect, deter, and interdict illicit trafficking;
- promote national export and transshipment controls; and
- manage and dispose of nuclear, biological and chemical weapons materials.

During the June 2003 summit at Evian, France, the leaders of countries, members to the Global Partnership, discussed some first outcomes and the nearest future action items in order to "prevent terrorists, or those that harbor them, from acquiring or developing nuclear, chemical, radiological and biological weapons; missiles; and related materials, equipment and technology." Together, they pledged to raise $20 billion over 10 years to support these goals. It should be noted that apart from the above technical goals that the Global Partnership seeks to achieve, there is an increasing trend towards broader international research collaboration to develop protections from biological agents that may be used by bioterrorists. This includes development of prevention, diagnostics and treatments as well as detection of possible terrorist attacks involving the use of biological agents.

While assessing very highly the above national and international efforts in the nonproliferation area, in strengthening confidence and transparency and countering bioterrorism, I would like to offer several recommendations for the action agenda:

1. In developing plans to counter biological and chemical terrorism, these should be based on the World Health Organization's recommendations on enhancing national preparedness and efficient response. An alert about possible deliberate acts should come from national security sectors whereas the responsibility for responding should lie with the public health sector as well as with veterinary, food safety and supplied water quality sectors.
2. There is an urgent need for long-term (at least 5 years) international programs to be launched on basic and applied research on the poorly known pathogens affecting humans, animals and plants, including assessment of the possible deliberate creation and use of genetically modified microorganisms. Special attention should be paid to the study of diseases with the potential to cause epidemics such as smallpox, Ebola fever, SARS, avian influenza H5N1, etc.
3. To ensure efficient implementation of the scientific research programs, an improved set of export controls for strains and related information should be adopted. At the same time, we should strengthen the monitoring over the possible "drain" of biological material and technology from the Global Partnership's research sector. The "human factor" should be paid special attention to. Unified requirements to storage, inventory of and work on pathogens should be adopted as well as unified biosafety and physical security standards supporting this type of research.
4. To implement the research programs and ensure preparedness for natural and deliberate outbreaks, it is proposed that regional Centers of Excellence for Bioterrorism and Emerging Diseases Research be established. It is important, however, that scientists from member-states to such centers be provided on-site access to conduct joint studies at these centers.

I wish to acknowledge the key role played by the staff of the Russian Federation Ministry of Industry, Science and Technologies, Russian Federation Ministry of Health, RAO BIOPREPARAT, Russian Federation Ministry of Foreign Affairs, Russian Academy of Sciences, Russian Academy of Medical Sciences, Institute of International Security of the Russian Academy of Sciences, those of the U.S. Department of State, ISTC, Cooperative Threat Reduction Program (DTRA/CTR), the U.S. Department of Energy, U.S. DHHS, CDC, NIH, U.S. NAS, USDA, CRDF in promoting US-Russian collaboration.

**References**

1. R. Preston. The Bioweaponeers. The New Yorker, March 9, 1998, p.52-65.
2. R. Preston. Bio-Warfare-Fiction and Reality, Genetic Engineering News, March 1, 1998, p. 6-39.
3. Chemical and Biological Terrorism. Research and Development to Improve Civilian Medical Response. Committee on R&D Needs for Improving Civilian Medical Response to Chemical and Biological Terrorism Incidents. Health Science Policy Program. Institute of Medicine and Board on Environmental Studies and Toxicology. Commission on Life Sciences. NATIONAL RESEARCH COUNCIL. National Academy Press, Washington, D.C. 1999.
4. Proceedings of the Eleventh Amaldi Conference on Problems of Global Security (November 18-20, 1998, Moscow, Russia). Moscow, "Nauka" 1999.