ORAVAX

ORAVAX, INC.
230 ALBANY STREET
CAMBRIDGE, MA 02139
TEL: (617) 494-1339
FAX: (617) 494-1741

Dr. Joshua Lederberg
Rockefeller University
1230 York Ave
New York City 10021

Dear Josh, 1 June 1993

After our meeting, I jotted down an outline of the rationale and implementation steps for converting research at Russian military institutes. This might be a starting place for further work by our subcommittee. The critical issue will be to line up funds for such a program. Funding should include enhancement of the CDC and USAMRIID research programs, as counterparts to those in Russian military institutes.

Best wishes,

Thomas P. Monath, M.D.
Vice President, Research & Development

Adjunct Professor,
Department of Tropical Public Health
Harvard School of Public Health

cc: Dr. John Steinbruner
The Brookings Institute
1775 Mass Ave NW
Washington DC 20036

Jo Husbands
CISAC
National Academy of Sciences
2101 Constitution Ave.
Washington DC 20418

Preliminary outline

Conversion of Military Institutes in the CIS to Peacetime Use

Objectives

1. Identify programs, facilities, and personnel in the CIS with expertise in research on dangerous biological agents

2. Redirect existing programs to meet public health problems associated with these agents.

3. Develop mechanisms for sustained funding of these activities

4. Retain the expertise of Russian scientists in research fields with which they are most familiar and prevent their defection to countries that might subvert their expertise to biowarfare activities

5. Develop links between these scientists/ institutes and counterparts in these fields in the U.S. and allied nations

6. Integrate a program of bilateral collaboration and research on dangerous biological agents into the braoder context of global surveillance and prevention of new, emerging, and re-emerging diseases

7. Promote transition of diagnostic test kits, vaccines, drugs, and vector control methods developed in this program into real-world clinical and epidemiological use, wherever possible as commercially viable products.

Background

With the demise of support for offensive biowarfare research activities within the Russian military-industrial complex, a number of military research institutes and their staffs are demoralized and underfunded. This creates a potentially dangerous situation for the West, raising the possibilities of subversion of previously controlled to uncontrolled activities, illegal selling of materials to third parties, and the defection of expert personnel to other countries.

The effort to convert military research and development projects to peaceful use depends principally on finding commercially viable alternatives. However, the biowarfare research program is focussed on diseases for which no private market exists for profitable commercial products. Although these 'exotic' infections have medical and public health importance, they are regional or localized in their distribution, have low natural incidence, and affect populations that cannot afford to pay for vaccines or other intervetions. For these reasons, research on the prevention and control of these diseases has been exclusively within the purview of

government agencies such as the Centers for Disease Control and the National Institutes of Health in the U.S. and similar agencies in a few other countries. Private industry in the U.S. or Europe has no interest in joint ventures and collaborative agreements with military institutes working on these exotic infections. Thus, conversion to peaceful research and development will depend on the creation of special programs and government funding.

In the military institutes, considerable inertia and resistance are inevitable to 'retooling' research programs and to retraining scientists to work in fundamentally different areas. A more acceptable approach would be to retain the expertise and to re-focus the knowledge gained in the biowarfare R&D program to activities that would promote public health, global surveillance and readiness. The deficiencies in the world's present capabilities to meet the threats posed by emerging and re-emerging infectious diseases have been repeatedly emphasized. What better cadre of experts and facilities could be found that those specifically devoted to research on dangerous biological agents?

Implementation steps

1. The American and Russian Academies should take the lead in promulgating a plan for implementation. The plan needs to be initiated by the U.S. side, as it is unlikely that our Russian counterparts have a perspective of what kind of proposal would be acceptable and fundable in the U.S.

3. A working subcommittee should be charged with drawing up a specific implementation plan. This group would consist of CISAC members and outside members from DHHS.[1]

4. An inventory of expertise, facilities, potential products (vaccines, diagnostic kits, etc.) in CIS military institutes would provide a basis for such a plan. Such an inventory would be greatly facilitated by site visits to the institutes themselves.

5. Prioritization of specific R&D efforts would be based on

i) Existing public health needs

Examples: Brucellosis, emerging as a major human health problem in the Middle East; Lassa fever, a regional public health problem of considerable magnitude in West Africa; tick-borne encephalitis, a significant (and uncontrolled problem) in eastern and central Europe; hemorrhagic fever with renal syndrome, a major endemic/epidemic disease in the Far East and the Balkan region; and *Legionella*.

ii) Potential emerging disease threats:

---

[1]Suggested names from DHHS: D.A. Henderson; C.J. Peters (CDC).

Example: Ebola virus disease, which caused emerged as a new disease in epidemic form in 1976 and reappeared in sheep's clothing in Reston in 1990.

iii) High-profile diseases in the biowarfare context.

Examples: anthrax, plague, tularemia, Q fever for which improved vaccines are clearly needed

6. Goals of the research effort would include the following:

i) Development of improved rapid and early diagnostic tests, including kits for distribution and use in endemic areas

ii) Development of vaccines, antimicrobial and antiviral drugs for the prevention and treatment of these infectious agents

iii) Investigation of disease outbreaks on the request of national and international agencies. This implies creation in advance of research teams that could be deployed to investigate the transmission, clinical features, pathophysiology, pathogenesis, and treatment of emerging diseases.

iii) Development of collaborations with national and academic groups in developing countries where these diseases are endemic, in order to establish longitudinal surveillance and research programs.

iv) Development of a routine information network, whereby research progress and epidemiological information would be reported to national and international agencies.

iv) Through field research on disease incidence and transmission, development of epidemiological 'test beds' where new diagnostics tests, vaccines, and drugs could be tested to establish their efficacy in controlled trials.

7. Transition of diagnostic tests, vaccines, and drugs to clinical development, including pilot lot production sufficient to conduct experimental and field studies in humans.

8. Establishment of a system of technology transfer and training of individuals engaged in research and public health activities.

9. Liason with private industry to assure that commercially viable product opportunities and new inventions with commercial potential are identified.

Funding issues

Funds would be sought from the Nunn-Lugar appropriation. Funds might be administered by DHHS, with CDC as the lead agency for establishing CRDAs with Russian institutes. Some funding should be used to enhance existing research programs at CDC and USAMRIID, which will serve as US counterparts to Russian military institutes. Allocations should recognize the need to establish subcontracts with overseas laboratories in developing countries, as part of the effort to create a global surveillance network.

The amount of funding must be clarified by an inventory of existing Russian programs and an assessment of the value of supporting them. We estimate that funding requirements would be in the range of $15-30 MM/year. Enhancement of CDC/USAMRIID programs would account for 15% ($2.25-4.5 MM) of the total.

T.P. Monath, M.D.
1 June, 1993