Symposium on Development of Vaccines for Viral Infections
(December 12-14, 1994)
Koltsovo, Novosibirsk region, Russia

Introduction:

A symposium on development of vaccines for viral infections was held on December 12-14, 1994 at the State Research Center of Virology and Biotechnology "VECTOR." The meeting was organized by the International Science and Technology Center (ISTC) with the help of VECTOR. The main purpose of the symposium was to bring together Russian and foreign experts in focussed areas of viral vaccine development in order to improve VECTOR proposals and planned projects to the ISTC. The agenda for the scientific program is attached (Attachment 1). Foreign participants included eight experts from the European Union and three delegates from the United States. Japanese experts were also invited but were unable to attend. The list of delegates, including 6 Russian experts invited from Moscow, is attached (Attachment 2). A large number of VECTOR personnel were also involved in the symposium via presentations, discussions, and tours of VECTOR facilities.

December 12, 1994:

The first day of the symposium featured a plenary session composed of more general presentations on the central topics of the symposium. Academician Sandakhchiev, General Director of VECTOR, opened the symposium with a welcome to the participants. A copy of his remarks is attached (Attachment 3). Professor Fasella, the current Chairman of the ISTC Governing Board, followed with presentation on the status of the ISTC. He noted that 93 projects, costing more than $47 million, have been approved for scientific projects in the Russian Federation and Georgia. He stated that projects involving vaccine development and other medical and health conversion topics have a high priority.

The technical presentations began with a talk by Dr. Vinogradova, Head of Department of the State Committee of Epdemiological Surveillance of the Russian Federation. She discussed the past and current state of health in the Russian Federation with respect to viral infections. She noted that earlier successes took place in reducing polio and measles, but that the current poor economy has led to a general increase in viral infections throughout the Russian Federation. She noted the current serious level of Hepatitis A and B infection and attendant health threats to the population, especially to children. The need for increased vaccination was described (see Attachment 4).

A talk on the side effects and immunological safety of vaccines was presented by Professor Medunitsin, Director of the Institute of Standardization and Control of Medicinal Immunological Preparations (RGIST). He reviewed the possible side effects of using vaccines and discussed the safety measures taken to reduce the chances of these effects (see Attachment 5). The Russian Federation requirements for obtaining high quality vaccines were presented by Professor Bektimirov, Deputy Director of RGIST. He pointed out that RGIST acts like the FDA in the US to inspect batches of vaccine and manufacturing facilities. The control process used in the Russian Federation for development and production of vaccines is discussed in his attached paper (see Attachment 6).

The regulations for immunological medicines in the European Union were presented by Dr. Pletshette, Commission of the European Communities, and Dr. Jepsen from the Office of International Health of Denmark. They brought a full copy of these regulations to the symposium and gave them to VECTOR. The regulations include those related to safety, testing quality, and marketing. They discussed the quality assurance program used in the EU countries that focusses on good manufacturing practices combined with quality control. They advised the Russian producers of vaccines to start with lower cost training and general upgrade of personnel to be followed by renovation of facilities.

Dr. Rick Smith, from Connaught Laboratories in the US, reviewed the good manufacturing practices advocated by the FDA in the US. He discussed the need to constantly improve under the US practice, based on the fact that a new idea quickly becomes the new standard. He said that the FDA inspects each laboratory at least every two years.

The final presentation of the plenary session was given by Academician Sandakhchiev. He discussed the topic of conversion of VECTOR to peaceful technologies from their former involvement in defense activities. He detailed the diverse capabilities of VECTOR to develop and produce vaccines against viral infections (see Attachment 7).

In the afternoon, visitors to VECTOR were allowed to visit several of their facilities, including the laboratories concerned with development of vaccines against Hepititis A and measles, a laboratory for study of HIV, the laboratory for biological and technology control, and the area where production of drugs and test systems is being prepared. Several people also visited the nursery for laboratory animals.

December 13, 1994:

The second day of the symposium was devoted to detailed discussion of two approved ISTC projects for development and production of Hepatitis A and measles. Two other proposals for (1) development and production of Hepatitis B vaccine and (2) for clinical trials of new vaccines were also discussed. These discussions were carried out in a workshop format. The proposed Russian project manager gave a prepared talk followed by detailed interchange of ideas and comments by working group participants.

Inactivated Hepatitis-A Vaccine:

A prepared talk was presented by Dr. Maidaniuk, Head of Department at VECTOR. He discussed the virus strain, the production procedure, and formulation and quality control of the final virus (see Attachment 8). Issues discussed in the workshop included the cell line proposed based on the kidney of the African green monkey. Western experts suggested that a different cell line based on the human diploid fiberblast would give VECTOR a better market opportunity because this is the cell line used in the West.

The second session speaker was Dr. Vinogradova, Head of Department from the State Committee of Epidemiological Surveillanve of the Russian federation. She discussed the requirements and methods of control of the quality of Hepatitis-A vaccine in Russia (Attachment 9). She noted that VECTOR and RGIST have tested a series of vaccines against Hepatitis-A. The triple scheme of vaccination has been found to be optimum. The issue of proposed vaccinations of children was raised. She noted that no vaccination of children is done before completion of trials on adults. They will use lesser concentrations for children.

The Western experts expressed general support for implementation of this project, under the conditions of having collaborators from the European Union and the US involved. It was also suggested that one or two people from RGIST should participate actively in the work.

Live Measles Vaccine:

Dr. E. A. Nechaeva, Head of Department at VECTOR, gave a presentation on the elaboration and production of a live measles vaccine (Attachment 10). She described the vaccine strain Leningrad-16 used in Russia in the production of the measles vaccine. She described how mass vaccination against this killer of children began in Russia in 1967. The project will develop and produce an oral vaccine preferred for children and without the possibility of hepatitis-B or HIV transmission through needles.

Professor Popov, Head of Department from RGIST, discussed the situation with respect to measles vaccine in the Russian Federation (see Attachment 11). He mentioned that Russian measles vaccine is currently exported to several developing countries, including Vietnam, Brazil, and Peru. Tests have been conducted at her institute that confirm the stability of the basic vaccine strain for many years.

An issue raised during this session included the need to characterize the Russian strain so that it can be compared to strains on which other vaccines around the world are based. Some doubts were also expressed about the efficacy of the delivery system for the oral vaccine.

The Western experts generally supported initiation of the project, subject to independent and parallel analysis of the strain in an EU laboratory and tests to determine if the strain would actively work once it reaches a receptor in the gut. Failure to prove out the efficacy of the oral delivery method would seriously compromise the project, and would probably eliminate support for later phases of the proposed work.

Hepatitis-B Vaccine:

Dr. Muratov, a scientist at VECTOR, made a presentation on creation and production of the recombinant vaccine against Hepatitis-B (see Attachment 12). He described the VECTOR work with the Vacinia virus. He mentioned that for the live vaccine, the recombinant protein is active in the antigen-presenting cells, reliably introducing a T-cell response. He saw the proposed project as the opportunity for them to organize a large scale production of a inexpensive, effective, and innocuous vaccine against Hepatitis-B in an oral form.

Dr. Shalunova, Senior Scientist at RGIST, discussed the situation with respect to Hepatitis-B vaccine in the Russian Federation (Attachment 13). She also reviewed the worldwide problem of Hepatitis-B infection and the need in Russia to produce low-cost, highly-effective vaccine that overcomes public resistance to vaccination.

Western experts raised several issues: They see a problem with possible dispersion of the live virus in the environment. They see possible exclusion of people who received smallpox vaccinations. Some felt that it is also difficult to judge whether there might be side effects. One recommendation was to include the core protein in a vaccine construct suitable for vaccination. The Russian scientists see a vaccination program as having many drawbacks and think an oral vaccine is still preferrable.

Clinical Trials of New Vaccines:

The possibilities of clinical trials of new vaccines at VECTOR was presented by Dr. Netesov, Deputy Director of VECTOR. He discussed the capabilities of the P-3 facilities at VECTOR to be used in the clinical trials of new vaccines, in particular against diarrheal diseases, especially cholera (see Attachment 14).

Western experts raised issues concerned with the proposed clinical trials and the current adequacy of the VECTOR facility. They made the following recommendations: To extend the immunological investigations, especially concerning the T-shell immunity parameters of volunteers during and after vaccination. It is also necessary to include into the list of equipment some small equipment for measuring the cell immunity parameters and the expenses for training of VECTOR specialists with modern methods. To make marketing investigations for finding additional offers for vaccine testing. To extend the facilities for immunological work in P-3 and increase the equipment for blood and urine analysis. To add the position of Biosafety Control Officer for the trials and a Bookkeeper.

December 14, 1994:

The third day of the symposium was devoted to a talk on production of test systems and tours of Russian Academy of Science Institutes in the area.

Dr. Zaitsev, Deputy Director of VECTOR (Attachment 15), discussed production of test systems and research reagents for the diagnosis of viral diseases and perspectives in their development. Additional remarks were provided by Professor Vorobiova, Head of Department of RGISK. The range of testing and diagnostics is very broad at VECTOR, including those for HIV 1&2, Hepatitis A, B, C, and D, measles, herpes, syphilis, and many others. VECTOR hopes to expand its production facility in 1995 and receive a European certification in 1996. They hope to expand their sales thereafter in several countries.