MCMR-UIZ-E 24 January 1997

INFORMATION PAPER

SUBJECT: Orthopoxvirus Genome Project. Dr. S. N. Shchelkunov, Principal Investigator

1. (U) The National Academy of Sciences site visit team which visited N.P.O. Vector in December 1996 rated a total of ten research proposals on the criteria of scientific validity, technical feasibility, and established linkages with U.S. investigators. An additional factor was the potential relevance of the proposed research to past, offensive biological warfare activities, and the possibility of successful conversion to peaceful purposes. The orthopoxvirus genome project scored very high according to these criteria and was one of two projects recommended for immediate funding by the team. From a BW conversion and defense perspective, this project is ideal in that it engages the appropriate Russian scientists and redirects their research objectives, while fostering direct exchange of scientific information among collaborating labs to include both the US DOD and HHS. If successful, this approach should lower the veil of secrecy and suspicion regarding the possible continuation of an offensive BW program. Conversely, if true transparency is not achieved, it would be a cause for continuing concern.

2. (U) While oral presentation of this proposal was targeted to cowpox, discussions extended to include the need for sequence information on other pox viruses, including monkeypox from the current outbreak in progress in Zaire, and perhaps others such as camelpox, which also infects humans and is thought to be the most closely related to smallpox. The proposal in the briefing packet emphasized monkeypox virus. As one of only two WHO collaborating centers for pox viruses in the world, the Vector group is well suited to conduct the studies proposed. They have a long-standing history of active collaborations with CDC, and the work to be done will clearly build on these past accomplishments and make effective use of the specialized skills and experience of the Russian staff. Sequence analysis should facilitate development of species-specific diagnostics based on PCR. Comparison of monkeypox virus genomes with variola may reveal substantial duplication of gene functions, thus contributing essential information relevant to the planned destruction of variola in 1999. Further, understanding of structure/function relationships for poxvirus genomes can be expected to provide insight into rational design of effective antiviral drugs and therapeutic strategies. It is hoped that an atmosphere of trust will be established, so that it would be possible for DOD investigators to travel to Novosibirsk for the purpose of testing candidate antiviral drugs against smallpox virus in cell culture and perhaps in animal models. Studies with infectious smallpox virus would be much more difficult to execute in the limited BSL-4 facilities at the CDC.

3. (U) Dr. Shchelkunov, the Principal Investigator, is a very talented scientist who speaks excellent English and is fully capable of conducting the studies as proposed. There were some concerns expressed by the representative from Biopreparat that the results anticipated might be "sensitive, requiring some level of classification." This is incompatible with a fundamental objective of this program, which is to achieve true transparency. Thus, if the Russian approval authorities accept this proposal, an additional layer of secrecy will have been removed. Political issues aside, the proposal should yield important information about virulence attributes of a significant class of viral pathogens, and insight into strategies to effectively diagnose and control these infections through improved immunization, antiviral drugs, and other countermeasures.

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