Preliminary Agreement Reached on U.S.-Soviet Space Cooperation

High-level U.S. and Soviet negotiators, meeting in Washington, D.C., during the week of 27 October, have settled on the framework for a new bilateral agreement on space cooperation. The agreement has no formal status as yet. However, President Ronald Reagan and Soviet General Secretary Mikhail Gorbachev are expected to sign it some time in 1987—if and when they ever meet again for a summit conference.

A new bilateral agreement would revive a tradition of U.S.-Soviet space cooperation that has been in limbo since 1982, when the Reagan Administration refused to renew a previous agreement in protest against the imposition of martial law in Poland. Informal exchanges have continued since that time on a scientist-to-scientist basis, as when several U.S. scientists were invited to participate in the Soviet VEGA mission to Halley's comet. But without a formal mechanism, say researchers, such exchanges are limited and ad hoc at best.

The Washington document accordingly identifies 16 space activities where cooperation would be useful. For example, Soviet researchers might be included in the scientific teams for the U.S. Mars Observer mission, now scheduled for the early 1990's, while U.S. researchers could likewise be included in the science teams for the Soviet Mars/Phobos and Mars/Vesta missions, which are planned for about the same time. Other proposals include a coordinated study of Venus; the use of the U.S. Deep Space Network to track Soviet spacecraft; and the exchange of medical data gathered from Mir/Salyut and space shuttle flights.

What the agreement does not have, however, is any reference to new missions—certainly nothing on the scale of the 1975 Apollo-Soyuz Test Project. As one observer points out, the agreement was "as bland as they could make it." In part this was because the U.S. negotiators had no authority to talk about missions that have not yet been approved. Thus, for example, they had to reject a Soviet proposal for a joint, unmanned mission to return a sample from the surface of Mars. But the blandness also reflected the Defense Department's concern that a joint space mission might create unacceptable technology transfer problems. Indeed, some officials at the Pentagon remain bitterly opposed to any kind of space cooperation, on precisely these grounds. On the other hand, the Defense Department was represented on the U.S. negotiating team, and has agreed to the final document; officially, at least, the technology transfer objection has been put to rest.

Reagan's interest in U.S.-Soviet space cooperation was apparently kindled on 30 October 1984, when he enthusiastically signed a Senate resolution on the subject sponsored by Senator Spark Matsunaga (D–HI). In July 1985, Secretary of State George Shultz accordingly raised the subject with Soviet Foreign Minister Eduard Schevardnadze. By July 1986, after a cool initial response, the Soviets had warmed to the idea and were ready to talk. In September, General Lew Allen, director of the Jet Propulsion Laboratory, took a technical delegation to Moscow to help lay the groundwork. And in October, the final negotiating teams were led by John Negraponte, assistant secretary of state for oceans and international environmental and scientific affairs, and Alexander Piradov, ambassador-at-large from the Soviet Ministry of Foreign Affairs.

Although the current agreement does nothing to address the question of new joint missions, many space scientists are hopeful that, once it is signed, it will provide a framework for more ambitious plans. The National Aeronautics and Space Administration, for example, has begun some preliminary studies for a joint Mars sample return mission with minimal technology transfer. In any case, Roald Sagdeyev, director of Moscow's Institute of Space Research, has said publicly that he wants to have a Mars sample return by the end of the century. As one U.S. scientist says, "Sooner or later, some Administration is going to *have* to consider a Mars sample return." ■

M. MITCHELL WALDROP

Overseas Field Tests Under Fire

Reports of American scientific involvement in field tests of recombinant animal vaccines conducted overseas are stirring up the debate in government and scientific circles over regulation of biotechnology. The Pan American Health Organization (PAHO), aided by the Wistar Institute of Philadephia, in July began a test of a recombinant rabies vaccine in Argentina. And two Oregon State University researchers in April started tests in New Zealand of a prototype method for constructing an array of animal vaccines. The two experiments appear to have been successful.

The plans for conducting the tests abroad also were cited in various publications, and the experiments are generally considered to have posed little risk to animal and human populations. However, the tests have aroused controversy because they come at a time when American regulators and scientists are grappling over regulations governing field testing of genetically altered organisms and plants. Two fundamental questions related to the application of genetic engineering techniques in agriculture remain unresolved: what constitutes a "release" of an organism into the environment; and when is an engineered organism considered "contained" for experimental purposes?

The Argentine test sparked protests largely because neither PAHO nor Wistar obtained explicit approval from the Argentine government before proceeding. The Oregon State University experiment, which was okayed by the New Zealand government, was conducted overseas because of the regulatory uncertainty that has plagued agricultural applications of biotechnology in the United States.

The Boston-based Committee for Responsible Genetics has charged that the two overseas experiments represent an effort to circumvent domestic regulations. The accusation was leveled on 13 November at a committee-sponsored conference devoted to setting a political agenda for biotechnology regulation. A House science subcommittee on investigations and oversight is considering holding a hearing next month to examine the controversy.

David T. Kingsbury, an assistant director at the National Science Foundation and head of the federal government's effort to coordinate regulation of biotechnology, has criticized Wistar and PAHO for not informing the Argentine government about the experiment until after it had begun. Kingsbury further speculated that regulations in the United States may be forcing researchers to conduct experiments overseas.

But Warren Cheston, Wistar's associate director, says Kingsbury's speculation, which appeared in the *New York Times*, "just is not true." U.S. rules governing the conduct of biotechnology experiments never were a factor in Wistar's decision to join in the experiment, Wistar officials say. The test was conducted in Agentina, Cheston says, because of interest expressed by health officials there and the high incidence of rabies in cattle in the region. Relatively few cows

contract rabies in the United States. In an interview with *Science*, Kingsbury agreed there was reason to test the vaccine in Argentina where rabies is often transmitted to cattle by vampire bats.

Sponsored by PAHO, a United Nations agency, the Argentine experiment involved the inoculation of cattle with a recombinant vaccine produced by splicing a single gene from a rabies virus into vaccinia virus. The aim was to trigger an antibody response in the inoculated cattle to the protein produced by the rabies virus gene. In the test, carried out at a PAHO facility in Azul, 20 uninoculated animals were isolated in a shed with the 20 inoculated cattle. The animals' four caretakers previously had been immunized with a vaccinia virus.

Daniel Epstein, a spokesman for PAHO in Washington, says that "in retrospect it would have been advisable for us to have informed Argentine officials of the experiment, and not treat it as a routine matter." The Argentine government was not notified until after the experiment was completed.

Cheston says that because PAHO was leading the experiment, Wistar did not seek to consult with the Argentine government, which objected to the experiment being done without formal notification. "We were a little naive as I think scientists frequently are," admits Cheston. Wistar's role included designing the experiment and providing the vaccine—an effort led by Hilary Koprowski, the institute's director. PAHO personnel administered the vaccine and analyzed blood samples.

The purpose of the New Zealand experiment, in contrast, was not to test a vaccine for a specific ailment, says Alvin W. Smith, a professor at Oregon State's College of Veterinary Medicine. Rather, it was a modeling exercise designed to determine whether a recombinant vaccinia virus containing genetic material from another virus would produce an antibody response sufficient to neutralize the virus in a diseased animal.

In the New Zealand test, a gene from a common animal virus, Sindbis, was inserted into the vaccinia. Some 37 calves, 16 chickens, and 4 sheep were involved. Serum samples from the control groups did not reflect any transmission of the recombinant vaccinia virus from inoculated animals. The experiment was conducted by Smith's colleague at Oregon State, Edward Wedman, who worked with researchers in New Zealand. Wedman also got approval to use U.S. Department of Agriculture (USDA) research funds in the experiment, which may lead to production of a vaccine to combat foot rot in sheep.

As for Smith and Wedman's decision to conduct their test in New Zealand, Smith says that 18 months ago there was no telling how long USDA would take to okay the experiment. James Glosser of the Animal and Plant Health Inspection Service says that the test might have gotten approved quickly given the nature of the undertaking. Smith says that if he were starting today, he would try to conduct the test in the United States because the regulatory process has improved. ■ **MARK CRAWFORD**

Harvard Researchers Retract Data in Immunology Paper

Last spring, researchers from Harvard's Dana-Farber Cancer Institute reported the discovery of a potentially exciting new molecule that appeared to amplify the vital T-cell activities that are necessary for many immune responses (*Science*, 7 March, p. 1118). In a letter in this issue (p. 1056), they are retracting that paper. The molecule, a lymphokine called interleukin-4A (IL-4A), is not real.

"The data are not reproducible," senior author Ellis L. Reinherz told News & Comment. "We need to set the record straight so no one tries to characterize a molecule that doesn't exist." The data apparently were tampered with. The extent of the problem is being investigated by an ad hoc committee of scientists from the Dana-Farber and Harvard Medical School.

The *Science* paper was coauthored by Neil E. Richardson, a graduate student, and Claudio Milanese, a Ph.D. from Turin, who was working in Reinherz's laboratory but has recently returned to Italy. A six-author paper on IL-4A published in the *Journal of Experimental Medicine* is also being retracted. Unpublished manuscripts have been withdrawn from *Science* and the *Proceedings of the National Academy of Sciences*.

IL-4A was reported to be a novel "lymphokine" that stimulates resting lymphocytes. (Lymphokines are any of the various factors involved in stimulating the growth or development of immune cells. Perhaps the most well known of this class of substances is interleukin-2, which is being used experimentally in patients with cancer and with AIDS.) In their *Science* paper, the authors reported that IL-4A induces interleukin-2 receptors.

Problems with the IL-4A data came to light only within the past several weeks when researchers in Reinherz's lab were unable to continue IL-4A experiments after Milanese's return to Italy. When no technical problems were found to explain why the experiments were suddenly failing to work, Milanese, who had been doing the biological assays, was asked to come back to Boston to help figure things out.

Shortly thereafter, it was decided that a full review of the situation was called for. Baruj Benacerraf, president of the Dana-Farber, acted promptly to establish a committee and to notify appropriate officials at Harvard and at the National Institutes of Health, which was funding the research. Notification of NIH is now required in cases in which scientific misconduct has been alleged. Mary Miers of NIH told *Science* that Harvard has submitted a "well-defined" plan for investigating the case.

According to Benacerraf, Milanese has "admitted" that the data are not valid in a letter to Reinherz "which is in our possession." Even so, Benacerraf says, "I don't take that as proof until our committee has reviewed everything."

In a telephone interview from Italy, Milanese acknowledged writing to Reinherz to admit he manipulated data. In reference to IL-4A he said that at first "I thought it was true. Then the cells stopped producing. There was a lot of pressure in the lab and I didn't have the courage to tell them." The problems apply only to the IL-4A research, Milanese told *Science* in reply to a question.

Reinherz and others decline to discuss the case in any detail, pending the outcome of the investigation, which is being headed by Stuart Schlossman of the Farber. David Kiszkiss, research director of the institute, says the committee will "look into the circumstances leading to the retractions. We don't want to say something now that isn't the full truth." Kiszkiss predicts that "If the story is a fairly simple one, we'll probably be able to wrap this up in a few weeks, perhaps a couple of months." Meanwhile, says Benacerraf regarding the immediate retraction of the IL-4A data, "The scientific record has to be corrected quickly." ■

BARBARA J. CULLITON