On Several Issues in the Space Life Sciences

On April 26, 1993, Space Studies Board Chair Louis J. Lanzerotti and Committee on Space Biology and Medicine Chair Fred W. Turek sent the following letter to Dr. Harry Holloway, associate administrator for NASA's Office of Life and Microgravity Sciences and Applications.

At the request of then Acting Director of Life Sciences, Joseph Alexander, the Committee on Space Biology and Medicine has examined and discussed four separate issues of concern to NASA and the Life Sciences Division and has developed comments and/or recommendations on each. Attachments A through D contain the committee's detailed conclusions and recommendations on (1) the use of research animals on Spacelab Life Sciences-2, (2) peer review of research proposals and programs, (3) optimizing the scientific benefits of the U.S./Russian Shuttle/Mir Program, and (4) Russia's biosatellite program (Bion). Following is a brief summary of the committee's thoughts on each.

USE OF RESEARCH ANIMALS ON SPACELAB LIFE SCIENCES-2

The use of animals in research has been of fundamental importance to the progress that has been made in biology and medicine. Integral to the scientific success of the upcoming Spacelab Life Sciences-2 (SLS-2) mission will be the use of rodents both as controls on the ground and in-flight as subjects of experiments. Some of the rodents must be sacrificed in space. The results of these studies will, for the first time, allow direct comparison between tissues exposed solely to microgravity and those obtained from ground-based controls, thus providing a basis for the development of measures to counter the effects of microgravity on humans in space. The Committee on Space Biology and Medicine fully endorses NASA's plans to use research animals on SLS-2 and subsequent missions. (See Attachment A.)

PEER REVIEW OF RESEARCH PROPOSALS AND PROGRAMS

Peer review of research proposals and programs is a long-standing practice of the scientific community that many regard as fundamental to ensuring the integrity of research findings and progress. Because of cultural differences and operational concerns, NASA's life sciences research has not always enjoyed the benefit of rigorous peer review. The Committee on Space Biology and Medicine recommends that *all* NASA-sponsored extramural and intramural life sciences research proposals and programs be subject to external peer review conducted at regular intervals. Further, in order to guard against a real or perceived conflict of interest, NASA Headquarters should regularly review the policy and management practices applied to extramural research programs by intramural contract and grant administrators and monitors. If any conflicts of interest arise, steps should be taken immediately to resolve them. (See Attachment B.)

OPTIMIZING THE SCIENTIFIC BENEFITS OF THE U.S./RUSSIAN SHUTTLE/MIR PROGRAM

Recognizing that the upcoming U.S./Russian Shuttle/Mir cooperative missions are largely demonstrations of international cooperation and engineering, the committee nevertheless believes that maximum benefit to the life sciences should also be a goal. The Committee on Space Biology and Medicine thus recommends that NASA Headquarters take all possible measures to ensure that the biomedical science activities on these missions be subject to rigorous peer review. The committee also recommends that NASA solicit assistance from the National Institutes of Health in choosing outside, independent experts to participate in the project to maximize the prospects of achieving scientific goals. The committee understands that there are numerous constraints and uncertainties surrounding this mission. (See Attachment C.)

RUSSIA'S BIOSATELLITE PROGRAM

Russia's biosatellite program provides the world's only free-flying spacecraft available for conducting extended-duration animal research in space. Over the past 20 years, the United States has provided support to U.S. investigators (approximately $2 million per year) to fly experiments on Cosmos series biosatellites. Current plans call for termination of U.S. participation in this program. Cognizant of both the advantages and disadvantages of the biosatellite program, the Committee on Space Biology and Medicine recommends that NASA maintain the option for future use of the Bion satellites by continuing its dialogue with the Russians about the various options available. In the meantime, NASA should survey its user community to ascertain the extent of the interest in using the Bion satellites and should formally evaluate the relative costs and benefits of different platforms for conducting animal research in space. (See Attachment D.)

In addition to requesting an examination of the above four items, Mr. Alexander asked that the committee consider reviewing its 1987 research strategy, *A Strategy for Space Biology and Medical Science for the 1980s and 1990s*, to assess whether that strategy requires augmentation and whether it accurately reflects the committee's current views and recommendations for NASA's space biology and medicine research program. The committee has discussed this request and plans to begin addressing it at its Spring 1993 meeting. We will keep you informed of our progress.

ATTACHMENT A

Use of Research Animals on Spacelab Life Sciences-2

Unique insights into modern medicine have been achieved through the humane use of animals in research. To enable the goal of long-duration human presence in space, we must continue to rely on animal experimentation to determine the consequences of, and develop countermeasures to, the effects of gravitational change. For NASA's life sciences program, and specifically the SLS-2 flight scheduled for August 1993, the use of research animals is critical to the scientific success of the mission. Some of the rodents must be sacrificed in space.[1] The Committee on Space Biology and Medicine agrees that this experimental protocol is well justified, for the following reasons:

- One of the most powerful tools available for the study of physiological processes in space and the development of measures to counter the effects of microgravity is animal research.[2,3] Marked advances in biology, physiology, and medicine have been made possible through careful, scientific study of animals in the laboratory.[4]

- The physiological consequences of exposure to microgravity have not yet been separated from those due to reentry forces because, in previous missions, tissue samples were collected only after return to Earth.[5-7] In contrast, SLS-2 will, for the first time, offer the unique opportunity to collect tissue samples in the microgravity environment according to the same procedures used in ground-based studies and will allow for direct comparison of the tissue samples collected in both environments.

- The Committee on Space Biology and Medicine fully endorses the use of animals on SLS-2 and subsequent missions, and it commends NASA for its plans to provide for their optimal care and treatment in flight. Animal subjects will be handled in accordance with the recommendations of the American Veterinary Medical Association panel on euthanasia and the recommendations of other panels.[8-11] Having a board-certified veterinarian on the mission will ensure the animals' welfare as well as the humane collection of animal tissue during the mission.

ATTACHMENT B

Peer Review of Research Proposals and Programs

During the past several years NASA has strengthened its peer review of both extramural and intramural life sciences research projects. While recognizing the constraints imposed on mission-oriented science, the Committee on Space Biology and Medicine believes it is nonetheless critical to extend the peer review mechanism to cover all NASA-sponsored biomedical research projects, proposals, and programs, including operationally oriented programs such as the Extended Duration Orbiter Medical Program, the Biomedical Monitoring and Countermeasures Program, and the U.S./Russian Shuttle/Mir Program. A rigorous peer review process is essential to ensure high-quality research projects and programs. In particular, the committee recommends that:

- Peer review of intramural research programs should take place at regular intervals. Peer review of the content and accomplishments of intramural programs should take place every 3 to 5 years. A process akin to that used by the National Institutes of Health (NIH) for assessing its intramural research programs would be appropriate. The review process used at the NIH has ensured standards of performance respected throughout the biomedical community.

- Intramural and extramural research projects and programs should be subject to the same peer review standards. Despite the constraints on operationally oriented projects, it is essential to maintain comparable standards for the review of intramural and extramural research projects and programs, to help maintain the quality of both.

- Review of intramural research programs should be conducted by qualified individuals not associated with that particular program. Intramural projects and programs should not be reviewed by investigators who are collaborators or are affiliated with the programs being reviewed, nor should they be reviewed by NASA grantees who are personally involved with the programs or projects.

- NASA Headquarters should regularly review the policy and management practices applied to extramural research programs by intramural contract and grant administrators and monitors. In an attempt to use its resources and intramural scientific personnel as effectively as possible, NASA often uses its scientists and group leaders as Research and Technology Operating Plan (RTOP) managers. This practice has led to concern and distrust in the research community about real or perceived conflicts of interest in the awarding and administering of contracts and grants. This practice also potentially compromises the independence of extramural NASA investigators in reviewing intramural projects and programs. Although the involvement of active researchers in

program management can be effective and productive, it also includes the potential for conflict of interest, and must therefore be carefully reviewed and monitored. Because even the appearance of a conflict of interest is counterproductive, it is incumbent on NASA Headquarters to institute procedures to regularly review the management of the research program and eliminate any conflicts. In the case of NASA's life sciences program, concerns have been raised by respected members of the community. The Committee on Space Biology and Medicine strongly urges the director of the Life Sciences Division to institute a procedure to regularly review the administration of the research program. If any conflicts of interest are discovered, NASA should take immediate action to resolve them. Such procedures will strengthen both the program and its administration.

- NASA should adopt the type of program administration that is used so effectively by the National Science Foundation and the National Institutes of Health, whose program officers have no direct personal interest in the research being conducted other than that it be successful. The program officer is judged on the basis of the overall quality and effectiveness of the research program he or she is overseeing.

ATTACHMENT C

Optimizing the Scientific Benefits of the U.S./Russian Shuttle/Mir Program

The Committee on Space Biology and Medicine recognizes that the U.S./Russian Shuttle/Mir Program was initiated primarily to demonstrate international cooperation and that the program has specific engineering goals. It further recognizes that life sciences activities performed as a part of this program face severe time constraints.[12] Within this context, the committee offers the following comments and recommendations with the goal of maximizing scientific achievements in the life sciences for both countries. These recommendations are consistent with recommendations made in *A Strategy for Space Biology and Medical Science for the 1980s and 1990s*[13] and *Assessment of Programs in Space Biology and Medicine—1991*.[14]

The committee has been informed by NASA that an investigative team will have responsibility for determining the overall scope and objectives of the program. Members of this team will be selected from a pool of investigators currently involved in operational issues associated with the human space program and from those with approved, peer-reviewed flight investigations. The committee also understands that NASA faces several unusual problems in trying to plan life sciences experiments because of the many uncertainties about the nature of the Shuttle/MIR program and the opportunities it offers for biomedical research. The unique opportunities that may arise from this program, however, require that NASA attempt to maximize the scientific return. Therefore the

committee recommends the following:

- Any opportunities to conduct basic biological experiments during the Shuttle/Mir program should be seized as a means to extend NASA's ongoing physiological studies on humans in space. The best outside experts should be solicited to advise the program.

- Acknowledging the constraints and uncertainties associated with this program, NASA Headquarters should nevertheless take all possible measures to ensure that biomedical science activities on this mission be subject to rigorous peer review.

- Outside independent experts should be brought into the project to maximize the likelihood of achieving scientific goals. These experts should be involved in the planning and in the experimentation and analysis phases of the program to ensure that the highest-quality science is performed. To accomplish this, the appropriate National Institutes of Health (NIH) institutes should be asked to recommend specialists. This approach would enhance interactions between NIH and NASA and would provide a model for additional future international collaborations.

ATTACHMENT D

Russia's Biosatellite Program (Bion)

Russia's biosatellite program includes a second-generation, free-flying satellite (Bion) of the Russian Cosmos series that allows for extended-duration animal experiments in space. The United States does not currently have this capability, nor does it have plans to fly biological specimens on free flyers in the future. Up to this point, NASA has sponsored U.S. scientists' use of Cosmos satellites for research, an activity cited as a major factor in the progress made in life sciences research over the last 5 years. However, because of budget pressures, this sponsorship was terminated at the time of the most recent Cosmos flight.[15,16] It appears that without international cooperation and support, the Russians may in fact terminate the biosatellite program.

The Committee on Space Biology and Medicine concludes that if Russia's biosatellite program is not canceled, Bion offers the following distinct advantages for the U.S. life sciences program: (1) Bion is currently the only vehicle available for extended-duration (30 to 60 days) animal experiments in space; (2) it provides a unique opportunity for follow-up research based on the most extensive set of existing U.S. data, collected on earlier missions, on microgravity's long-term effects on animal systems; and (3) it provides for continued, meaningful research in the period before a U.S. space station becomes available.

At the same time, the committee recognizes that Bion has cost uncertainties as well as the following severe limitations: (1) Available power limits the number and type of experiments that can be conducted; (2) problems associated with reentry may compromise the interpretation of some scientific data; (3) there is no opportunity to manipulate the payload in flight; and (4) the instability of the political and economic situation in Russia may compromise the future of the biosatellite program and jeopardize potential U.S.-Russian cooperative activities.

Having weighed both the advantages and disadvantages of continued U.S. participation in the biosatellite program, the Committee on Space Biology and Medicine recommends that:

- NASA should formally evaluate the relative benefits and cost-effectiveness of different platforms for animal research in space. Depending on the outcome of this analysis, NASA should consider providing research support in the 1995 life sciences budget for the biosatellite project.

- NASA should survey its user community to ascertain the extent of interest in the potential use of the Bion satellites.

- NASA should continue discussions with the Russians concerning potential U.S. use of the Bion satellites.

- NASA should indicate an "in principle" interest in the Bion project to the Russians in these continuing discussions.

[1]"Rationale and Protocol for Animal Sacrifice Onboard SLS-2 Mission," Communication from NASA Life Sciences Division, February 5, 1993.

[2]"Animal Use on the SLS-2 Mission," Presentation by Ron White, NASA Headquarters, to the Committee on Space Biology and Medicine, January 28, 1993.

[3]*A Strategy for Space Biology and Medical Science for the 1980s and 1990s*, Committee on Space Biology and Medicine, National Academy Press, Washington, D.C., 1987.

[4]*Science, Medicine, and Animals*, Committee on the Use of Animals in Research, National Academy Press, Washington, D.C., 1991.

[5]"Cosmos 1887 (Bion 8)," Special Issue, *Federation Proceedings, FASEB*, Vol. 4, No. 2, January 1990.

[6]"Cosmos 2044 (Bion 9)," *Journal of Applied Physiology, Special Issue*,

(Supplement) Vol. 73, No. 2, August 1992.

[7]*A Strategy for Space Biology and Medical Science for the 1980s and 1990s*, Committee on Space Biology and Medicine, National Academy Press, Washington, D.C., 1987, and *Assessment of Programs in Space Biology and Medicine—1991*, Committee on Space Biology and Medicine, National Academy Press, Washington, D.C., 1991.

[8]"1993 Report of the Panel on Euthanasia," *Journal of the American Veterinary Medical Association*, Vol. 202, No. 2, January 15, 1993.

[9]*Guide for the Care and Use of Laboratory Animals*, NIH Publication No. 86-23, U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Bethesda, Md., 1985.

[10]*Laboratory Animal Management: Rodents, A Report of the Committee on Rodents*, Institute of Laboratory Animal Resources, National Research Council, reprinted from ILAR News, Vol. XX, No. 3, 1977.

[11]"Position Statement on Use of Animals in Research," *NIH Guide for Grants and Contracts*, Vol. 22, No. 8, February 26, 1993.

[12]"U.S./Russian Shuttle/Mir Program," Presentation by Frank Sulzman, NASA Headquarters, to the Committee on Space Biology and Medicine, January 27, 1993.

[13]*A Strategy for Space Biology and Medical Science for the 1980s and 1990s*, Committee on Space Biology and Medicine, National Academy Press, Washington, D.C., 1987.

[14]*Assessment of Programs in Space Biology and Medicine—1991*, National Academy of Sciences, Washington, D.C., 1991.

[15]"Cosmos Biosatellite Program," Presentation by Frank Sulzman, NASA Headquarters, to Committee on Space Biology and Medicine, January 27, 1993.

[16]"Research Opportunities Using Cosmos Satellites-A User's Perspective," Presentation by Bernard Cohen, Mt. Sinai Hospital, to Committee on Space Biology and Medicine, May 14, 1992.