A letter writer warns that not enough safeguards are in place to protect the U.S. population from the release of harmful organisms from U.S. laboratories. A researcher emphasizes that NASA's funding of crystal-growing on the space shuttle contributed to the development of a promising flu drug. Human tissue engineers clarify their procedure in growing blood vessels. A method of testing wells in Bangladesh for arsenic poisoning is described. And a Hungarian scientist calls for the "appropriate balance between the discovery of new facts and finding their proper place and importance in the framework of science."

Uncontrolled Release of Harmful Microorganisms

At a recent colloquium held at the U.S. National Academy of Sciences in Washington, DC, there was intensive discussion of a wide range of applications of laboratory automation. These applications included methods for prevention and early detection of biological warfare agents, infectious diseases, and water and food supply contaminants. The main concern raised was the use of pathogens by terrorists or nations as a result of biological warfare. It is clear that U.S. Army authorities and the Federal Bureau of Investigation are able to predict the outcome of numerous scenarios regarding the hostile use of microorganisms. Also, it appears that we are well prepared to detect, respond to, and potentially prevent such threats.

Are there enough safeguards in place to protect the U.S. population from the release of harmful organisms from U.S. labs?

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However, a different type of threat, the release, either intentionally or unintentionally, of laboratory strains and genetically modified organisms, is underestimated. These organisms include natural, highly antibiotic-resistant commercial strains, as well as bacteria that were created either by genetic manipulations such as rapid DNA shuffling or by rationally designed point mutations. Such organisms can interact with human pathogens and can easily change the microbial diversity and ecology that we know today. We have already experienced an example of such release in the case of the antibiotic-resistant human opportunistic pathogen *Burkholderia cepacia*. This plant pathogen is used in agriculture as a biocontrol agent and in the bioremediation of toxic chemicals (*1*). *Burkholderia cepacia* is still released into the environment as a bioremediation agent, despite the fact that it is now recognized to be a cause of devastating infections in patients with cystic fibrosis (*1*, *2*) and in other vulnerable individuals (*1*, *3*), and its use in agriculture is controlled by the Environmental Protection Agency (*4*).

It is evident, therefore, that we need to create guidelines and safety measures that will prevent the uncontrolled release of microorganisms into the environment. In addition to the necessary guidelines, those involved in biotechnology should direct their attention to creating laboratory host strains that will survive only in controlled laboratory conditions. Bacterial and viral genetic manipulations that may influence our environment need to be restricted to such laboratory strains. Such measures should reduce the threat of the accidental release of harmful species into our ecosystem.

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Space-Grown Neuraminidase Crystals

David Malakoff's article concerning the science that will be conducted on the international space station (News Focus, 14 May, p. 1102), mentions a recent press release by the National Aeronautics and Space Administration (NASA) regarding influenza neuraminidase crystals that were grown in space. Malakoff interviewed me, and I clearly explained to him that crystals grown on the Mir space station produced the best x-ray diffraction data set in our laboratory at that time and were used to determine the 3-dimensional structure of N9 neuraminidase (*1*). This native structure was subsequently used for all of the University of Alabama, Birmingham, Center for Macromolecular Crystallography's (CMC's) drug complex structures, and still is today. In addition, we flew N2 and B-Lee-40 neuraminidase on the U.S. space shuttle. These crystals were used to determine several inhibitor-protein complex structures and to optimize the cryopreservation protocol used for all future neuraminidase crystals. In spite of my providing this information, Malakoff quotes Graeme Laver as saying that "the single space-produced crystal involved in the project was grown aboard Mir without NASA's help. 'And it had nothing to do with the drug's development. BioCryst's findings came from crystals I grew on Earth.'"

The CMC and BioCryst Pharmaceuticals worked as a team, sharing all information from this drug development project. It is incorrect to assert that the data and work performed by the CMC (using space-grown crystals) did not contribute to the scientific development of a useful clinical candidate drug. NASA's contribution to this project was substantial in terms of 10 years of funding support and crystallization of N2 and B-Lee-40 neuraminidase to support the drug design.

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Tissue Engineering

Dan Ferber ("Lab-grown organs begin to take shape," News Focus, 16 Apr., p. 422), describes our recent study (*1*) presenting the only human tissue engineered blood vessel (TEBV) that is both completely biological and strong enough to be implanted. The article, which compares our work with a study by Niklason and collaborators published in the same issue of *Science* (p. 489), states incorrectly that the human TEBVs we implanted in dogs had been lined with an endothelium. In fact, although TEBVs were routinely produced with a functional endothelium, we intentionally did not endothelialize the human TEBVs for xenografting because xenogeneic endothelial cells induce an acute rejection which leads to rapid thrombosis (24 hours). The

goal of this xenograft was to demonstrate suturability and short-term (1-week) mechanical stability under arterial pressure, but not blood compatibility. As mentioned in the article, 50% of the first six human TEBVs implanted were still functional after 7 days, which, when put in context, is quite an accomplishment. What were described as "blood leaks" were likely artifacts resulting from the aggressive anticoagulation protocol necessary in this setting. Although we could have seeded an autologous (canine) endothelium to increase the xenograft survival rate, we decided against it because the results would not have been relevant to the clinical setting, where, of course, only endothelialized autologous human TEBVs will be grafted. Our rationale appears to be supported by the paper by Niklason *et al.*, where a synthetic biodegradable graft seeded with bovine smooth muscle cells and lined with a porcine endothelium was implanted in a porcine model. The hybrid graft remained functional for 4 weeks, but the xenogeneic tissue was visibly rejected. Considering the different objectives, it seems inappropriate to compare graft longevity observed in the study by Niklason *et al.* with the longevity we observed.

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Testing of Water for Arsenic in Bangladesh

The discovery of arsenic in drinking water in Bangladesh has been described as "the biggest mass poisoning in history" (*1*). More than 80% of the population in the country now have access to drinking water supplied from hand-pumps dug over the previous two decades, and the discovery of arsenic in such water has dealt a direct blow to this "success story," threatening the lives of millions of Bangladeshis. Two challenges confront the government and other development agencies working in the country: testing the water supplied by hand-pumps for arsenic and identifying an effective, affordable, and sustainable mitigation procedure.

Arsenic victim

The testing of water supplied by hand-pumps, of which there are more than 2.5 million, is itself a formidable job. BRAC, a local nongovernmental organization, has tested a method for large-scale, field-level arsenic testing by training village-based community health workers (CHWs) (*2*) using a field kit. The kit, developed by the Asian Arsenic Network of Japan, determines the presence of arsenic in water through chemical reactions and works in the following manner: in groundwater, arsenic usually occurs as arsenite (As-III) and arsenate (As-V), and the kit reduces arsenate to arsenite by potassium iodide (KI) and stannous chloride ($SnCl_2$). The As-III is then reacted with zinc and hydrochloric acid (HCl) to produce arsenic gas. A color change from light-yellow to reddish-brown on bromide paper indicates the presence of arsenic in the water. Forty CHWs in a subdistrict previously known to be arsenic-affected were trained to use the kit. They then tested water from all 11,954 hand-pumps in 156 villages. Results showed that water from 93% of the hand-pumps was contaminated. A subsample of the water samples simultaneously tested in a government laboratory using a spectrophotometer confirmed the field testing in 92% of the cases. The cost of the testing was less than 50 cents per water sample, which is only a fraction of what it costs in a laboratory. This mass testing at the field level also aroused enormous awareness among the villagers about the arsenic problem. On the basis of this experience, BRAC is now working with the government and UNICEF to test the water supplied by all the 18,000 hand-pumps installed in the country in 1998.

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Limits of Scientific Growth

As one of the organizers of the International Forum of Young Scientists (a satellite of the World Congress of Science on 23 and 24 June in Budapest, Hungary), I hear more and more complaints from fellow researchers from all over the world about the increasing fragmentation of scientific knowledge. There is only a limited effort to achieve the appropriate balance between the discovery of new facts and finding their proper place and importance in the framework of science (*1*). Science itself is not self-integrating, and there are fewer and fewer people taking responsibility for "net-

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