search in academia, we pointed to "obvious exceptions, both in federal programs and in university tenure policies. Certainly the most powerful exceptions are in the many research programs conducted in the federal laboratories and in industry, where the goals...force vigorous and effective interdisciplinary work." Noonan's citation of work done by EPA laboratories themselves or in concert with other agencies strongly supports this point.

We certainly applaud the vigorous efforts by the EPA to broaden this perspective to the universities, in the face of what we continue to believe are formidable barriers, most prominently that of a regulatory agency supporting academic research that is fundamental, stable, of high quality, and with sufficient scale. This issue is not new and, indeed, since our article was published we have received a significant number of e-mails from researchers supported by EPA agreeing with our comments.

Finally, Noonan's metaphor of a "Potemkin village" is apt: The successes of U.S. research—including, of course, major advances on environmental issues—have distracted us from what are some substantial weaknesses, of the sort we described in our Policy Forum.

Norman Metzger
Executive Director, Commission on Physical Sciences, Mathematics, and Applications, National Research Council, 2101 Constitution Avenue, NW, Washington, DC 20418, USA. E-mail: nmetzger@nas.edu

Richard N. Zare
Past Chairman, National Science Board, Department of Chemistry, Stanford University, Stanford, CA 94305, USA. E-mail: zare@stanford.edu

C. elegans as a Model

Elizabeth Pennisi, in her excellent commentary "Worming secrets from the *C. elegans*" (News Focus, 11 Dec. 1998, p. 1972), states that "The first person to sense that the worm might take on such a prominent role in biology was molecular biologist Sydney Brenner." I am sure that Brenner would wish to acknowledge the role that Ellsworth C. Dougherty played in this matter. Dougherty originally described in 1949, " [a] new species of the free-living nematode *genus Rhabditis* of interest in comparative physiology and genetics" (*1*). From 1949 until his death in 1965, Dougherty, working primarily in Berkeley, California, promoted the use of *Caenorhabditis* as a model metazoan organism. He and his colleagues Hansen, Nigon, and Nicholas, in particular, established culture techniques, determined nutritional requirements, and identified genetic mutants to facilitate the research usefulness of this organism. In the early 1960s he introduced it to Brenner during one of Brenner's sojourns at Berkeley.

Much of this pioneering work is summarized in many publications and in two monographs (*2*). Dougherty's work provided a solid foundation for the accomplishments that Waterston, Sulston, and Coulson have achieved. The availability of the nucleotide sequence of *C. elegans* will open the prospect of exciting new insights for metazoan biology.

Paul H. Silverman
American Academy of Arts and Sciences, University of California, Irvine, CA 92697, USA

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Hot Zones

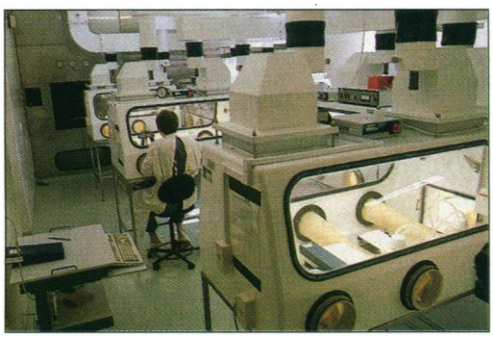
The public's perception of disease, especially infectious disease, changes as a function of perceived threat. Tuberculosis, scarlatina, diphtheria, and tetanus no longer cause the fear they did in my childhood. Conversely, anthrax and Ebola virus are usually described as "deadly," and we read in tabloids of "flesh-eating" microbes that can devour the infected. The solution to these "deadly" problems in the popular consciousness is to have "hot labs" in "hot zones" manned by spacesuit-clad personnel, as seen in films and on television.

The reality is that there are laboratories dedicated to containment of infectious agents, not only for human diseases but, perhaps more important, for plant and animal diseases. Such laboratories, as we know, are classified by the degree of isolation they provide, ranging from Biocontainment Level I (BCL 1) through BCL 4 (P4), which is the technologically maximum barrier between infectious material and the world outside.

Containment facilities were originally developed as a concept with the challenge of importing lunar samples that could have been contaminated with pathogenic extraterrestrial organisms. Because these early facilities were designed by engineers, hardware prevailed, in the form of laminar flow hoods, improved glove boxes, and air filtration systems. Before that time, containment was left to an investigator's discretion, with the exception of biological warfare facilities. Activities at these facilities were kept secret, although rumors of breaches of containment (and fatalities) have circulated. Industry has had a different class of containment, now referred to as Good Manufacturing Practices, that was designed to keep products from being contaminated.

The number of P4 laboratories that exist is unclear. A web site called ProMED-

mail (www.healthnet.org/programs/promed.html), which provides reports for infectious disease enthusiasts, has indicated there may be 24 or so worldwide, although some are still under construction.



Interior of P4 laboratory at Porton Down, United Kingdom

CREDIT: JAMES KING-HOLMES/SCIENCE PHOTO LIBRARY/PHOTO RESEARCHERS

Some are very well known, such as those at the U.S. Centers for Disease Control; Porton Down, United Kingdom; and Novosibirsk. Others, like those at the Centre International de Recherches Médicales de Franceville in Gabon or the national laboratory in Madrid, are less well known.

There is little doubt that, conceptually, P4 facilities are important and necessary to have. On the other hand, they should not be regarded as an object of prestige the way a national airline may be for a developing country. If the public believes that P4 facilities are their first line of defense for new or emerging illness, then the public must also be assured that their safety is at least as rigidly controlled as is that of the nuclear reactor industry. A spill in a poorly managed P4 facility could be far more devastating than Chernobyl or Three Mile Island.

At present, the standards for constructing P4 facilities are limited because local building codes, access to sites, and local laws and ordinances hinder international rule-making. Indeed, a private individual may construct a putative P4 facility in most countries and culture organisms that would be a threat to themselves and their neighbors with little trouble. Such seems to have happened in Iraq and elsewhere.

The renewed interest in bioterrorism has seemed to the public to be a reason for more P4 facilities. In fact, P4 facilities could do little after a terrorist act has occurred. On the other hand, P4 facilities provide a wonderful setting for producing potential weapons and should be considered with the same regard as nuclear weapon storage facilities.

Clearly, a central authority is urgently needed. P4 facilities have absolute requirements for personnel training, with the most emphasis on cleaning and maintenance personnel. P4 facilities must be thought of as a way of life rather than a collection of mechanical devices. An international regulating body needs to be created, and signatory nations should enter into an agreement as to the maintenance and use of P4 facilities, much as nations have agreed to biological warfare limitations. Equipment for furnishing P4 labs should also be regulated, just as equipment for plutonium technology is. There should also be some method for deciding how many P4 facilities are really needed and where.

Finally, there is an apparent shortage of capacity at some of the larger labs, and each new outbreak of a mystery disease results in more material requiring containment space. While some of this difficulty could be solved by housecleaning of irrelevant material or cultures, long-term solutions require increasing budgets and manpower for currently available facilities.

It should be the responsibility of every scientist to participate in this effort.

Cecil H. Fox
Molecular Histology, Inc., 18536 Office Park Drive, Montgomery Village, MD 20886, USA

U.S. Emission Permit System

We found both the article "Acid rain control: Sources on the cheap" (News Focus, 6 Nov. 1998, p. 1024) and the accompanying box "Pollution permits for greenhouse gases" (p. 1025) informative and generally correct. However, we disagree with the characterization of the tradable emission allowances as a "free-market approach."

The U.S. tradable emission permit system is more accurately described as a "constructed market" than a "free market." It did not evolve as a natural market out of the free play of economic interests. Rather, it is an institutional innovation invented by resource economists, promoted by environmental interests, and implemented by government to replace earlier command-and-control institutional arrangements.

A system of property rights and tradable permits for the management of pollution was first proposed by resource economists in the late 1960s. These early proposals were followed by a substantial theoretical and empirical literature. In the mid-1980s, the Environmental Defense Fund began to support a market-based approach to residuals management. These proposals received sympathetic attention from the U.S. Environmental Protection Agency (EPA) Administrator William Reilly, who had previously served as president of the Conservation Foundation. But