The Costs of Animal Research: Origins and Options

Linda C. Cork, Thomas B. Clarkson, Robert O. Jacoby, Diane J. Gaertner, S. L. Leary, Jeffrey M. Linn, Steven P. Pakes, Daniel H. Ringler, John D. Strandberg, Michael M. Swindle

Animal-based research comprises almost half of the portfolio of the National Institutes of Health (NIH). It is vital to the biomedical community but is encountering unprecedented challenges to its continued success. These challenges are related to technological advances in science and to specific aspects of the regulatory climate and costs of animal research. These are not abstract issues for the individual scientist. The costs for animal research may determine in which institution a scientist pursues his/her research and with whom he/she can, or cannot, collaborate. The National Allergy and Infectious Disease Advisory Council outlined many of these challenges in a resolution forwarded to NIH Director Varmus in February 1996. As scientists who deal with this issue daily, we highlight the origins and the potential solutions.

Much current animal-based research focuses on basic biological mechanisms or host-agent interactions and requires specific pathogen free, genetically uniform rodents, especially mice. Many are designer animals that offer a unique opportunity to understand the function of specific genes or to create rodent models that are susceptible to human pathogens. Animals with induced mutations may be unusually susceptible to infectious agents including some previously considered inconsequential. These designer rodents require intensive health monitoring and more sophisticated husbandry; as a result expenses for equipment and specialized animal care have increased significantly.

Historically, the NIH supported the infrastructure of animal resource programs as an essential component that protected federal investments in biomedical research. This support included grants to train veterinarians in specialties central to animal-based studies: research skills, laboratory animal medicine, and comparative pathology. Training grants now preclude substantive clinical training leaving a potential deficit in clinical support that can only be met by highly skilled professionals. Federal support for animal diagnostic laboratories (microbiology, virology, and pathology) also has been discontinued. Ironically, this has occurred as the need for diagnostic support to protect the health of designer animals has escalated. The animal diagnostic laboratories represented a financial partnership between the federal funding agencies and the biomedical community. As financial demands on institutions have increased, they find it difficult to fund these essential programs alone, despite their critical importance in support of animal health.

An additional hidden cost has resulted from the growth of organismal approaches to molecular genetics, especially utilizing the achievements of the Human Genome Project. This growth also has brought many scientists with little or no background in animal research to animal-based studies. These individuals often require training by animal resource staff and veterinarians to prepare them to perform animal experimentation appropriately and to comply with regulations governing animal welfare.

Animal welfare is a vital concern for the public and the scientific community; as a result, animal experimentation is heavily regulated. Regulatory agencies require extensive documentation of virtually all activities that involve animal use, entailing additional effort from investigators, administrators, and animal resource staff. Animal resource staff spend many hours reviewing required animal care protocols for institutional animal care and use committees, counseling and training scientists and their staff, providing veterinary medical care, monitoring compliance, and dealing with a myriad of details, inspections, and reports required by regulatory and accrediting agencies. Although regulations continue to proliferate, the cost: benefit ratio has not been adequately assessed scientifically, ethically, or financially by society, legislators, and regulatory agencies.

Probably the single most damaging action to affect the cost of animal research was the federal government's decision to consider research animal resource programs as "specialized facilities." This action required that all the costs of operating such facilities must be excluded from the institution's indirect cost recovery agreement and instead should be fully recovered from users. The rationale underlying this approach appears flawed, because other types of regulated research, for example, that using radioactive isotopes, are not treated in this fashion. Federal negotiators have implemented the "specialized facility" rule inconsistently in apparently comparable institutions. When it is applied, the direct costs of animal research soar—often more than doubling (*1*). Coupled with the federal government's increasing efforts to drive down the recovery of the indirect costs of research, the effect on an animal care program can be devastating. Ongoing efforts by the National Center for Research Resources (NCRR) to standardize the methodology for allocating costs of animal use are an important step as are the ongoing discussions with the Office of Management and Budget (OMB) that seek to redress this targeting of animal research. The draft for cost analysis and rate setting is available for comment until 12 May 1997 (http://www.ncrr.nih.gov/cost/costman.htm).

We have responsibilities for the oversight of laboratory animal programs in major research institutions. As investigative scientists we applaud the opportunities presented by animal research; as research animal program and animal facility administrators, we strive to find ways to achieve them. We cannot do this alone. We seek partnership with fellow scientists who use research animals, institutional leadership, an informed public, and the federal government. To remove penalties from animal research and benefit animal welfare, we recommend that the revised standards of cost allocation by OMB be

L. C. Cork, Chair, Department of Comparative Medicine, Stanford University School of Medicine, Stanford, CA 94305, USA.
T. B. Clarkson, Chair, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, NC 06511, USA.
R. O. Jacoby, Chair, Section of Comparative Medicine, and Director, Animal Resources Center, Yale University, New Haven, CT 06511, USA.
D. J. Gaertner, Director, Institute for Animal Studies, Department of Microbiology and Immunology, Albert Einstein College of Medicine, Yeshiva University, New York, NY 10033, USA.
S. L. Leary, Assistant Vice Chancellor for Veterinary Affairs, Washington University School of Medicine, Saint Louis, MO 63130, USA.
J. M. Linn, Director, University of Laboratory Animal Resources, University of Pennsylvania, Philadelphia, PA 19104–6021, USA.
S. P. Pakes, Professor and Chair, Division of Comparative Medicine, University of Texas Southwestern Medical Center, Dallas, TX 75235, USA.
D. H. Ringler, Professor and Director, Unit for Laboratory Animal Medicine, University of Michigan School of Medicine, Ann Arbor, MI 48109–0164, USA.
J. D. Strandberg, Professor and Director, Division of Comparative Medicine, The Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.
M. M. Swindle, Director of Laboratory Animal Resources, and Chairman, Department of Comparative Medicine, Medical University of South Carolina, Charleston, SC 29425, USA.

adopted promptly and that the designation as "specialized facilities" be removed from animal resource programs. Requiring institutions to allocate animal care costs comparably would create a level playing field; institutions could bench mark their costs and identify areas to improve efficiency based on local conditions. To further enhance animal welfare, we recommend that increasing funds be allocated to support animal health infrastructure especially for specialized animal populations.

We know of no national forum to exchange views or seek workable and timely solutions. A workshop planned by the NCRR is an important step in this direction. However, we believe that it is important that the scientific community be aware of the obstacles to continued productive animal-based research and join in overcoming them.

REFERENCE

1. *Federal Register* **60**, 7107 (1997).

Life-Sciences R&D, National Prosperity, and Industrial Competitiveness

R. Fears, M. W. J. Ferguson, W. Stewart, G. Poste

The importance of science and technology (S&T) as a catalyst in promoting national prosperity, improved health, and quality of life has long been cited as justification for investment in basic research and industrial R&D (*1*). Despite the dramatic economic and social benefits generated by S&T over two centuries of the industrial era, Vannevar Bush's vision of the endless frontier for research (*2*) has not yet yielded endless solutions for many in society.

Throughout the industrialized nations of the Organization for Economic Cooperation and Development (OECD), the relationship between science and society is in flux, with increasing political demands to forge closer ties between basic research and industrial applications to address societal needs. A recent paper in *Science* (*3*) referred to this trend as the "changing ecology of science" in which the principal challenge facing those responsible for science policy is how to prioritize S&T investments to optimize technology transfer, while maintaining a competitive science base in the face of constrained funding and escalating costs. We describe developments in science policy in the United Kingdom over the past 4 years that have imposed a major restructuring of the governmental policy apparatus for the review and funding of academic research and its linkage to the industrial sector.

We do not share the view (*4*) that a strategic policy for S&T is incompatible with excellence in life sciences and biomedical research or will inevitably lead to "short-termism" to meet the perceived avarice of financial and commercial constituencies. On the contrary, we believe that the denial that basic research can be assessed is counterproductive and unnecessarily alienates political constituencies involved in funding decisions.

The policy trends documented here are relatively recent, and it is too early to measure tangible achievements in terms of national goals. Nonetheless, the importance of developing innovative strategies and frameworks to capitalize on S&T and to develop coherence in public policy cannot be overstated (*5*).

Contestable Generalizations

It has become almost de rigueur in the United Kingdom, and elsewhere, to comment that the major impediment to industrial exploitation of science is the short-termism of industry and inadequacies in the management and comprehension of technology within executive boardrooms. These generalizations are questionable and dangerous. Excellence and mediocrity exist in both industry and academia, and national competitiveness demands excellence in both. In some sectors, industry scientists are world leaders. The pharmaceutical sector, for example, is outstandingly successful in the global marketplace. R&D expenditure by U.K. pharmaceutical companies accounts for 34% of national industrial R&D (*6*) and exceeds the life-sciences research funding provided by government and the medical charities. Pharmaceutical companies have also become leaders in life-sciences basic research such as genomics.

The assumption that the short-termist views of U.K. shareholders take precedence over patient investment for innovation can also be challenged (*7*). The United Kingdom has lagged behind the United States in the launch of new life-sciences companies with venture capital, but is ahead of continental Europe in the vitality of this sector (*8*). Whereas much remains to be done to infuse S&T into business degrees and the syllabi of other professions (such as law, accountancy, banking, and insurance) routinely involved in S&T activities (*8*), the United Kingdom also leads Europe in this regard.

In some parts of academia, there has been a delusional belief that every institute of higher education must become an international center of research excellence. Yet the expansion in the number of universities, following the recent U.K. reclassification of higher education centers, means that relatively few will achieve this status. Moreover, the capital investment for world-class competitiveness is daunting. The long-term effect of passive neglect of the science base infrastructure will be an inability to compete in the next century, when innovative technology products will be at a global premium. Neglect of an underpinning academic infrastructure implies a lack of appreciation by politicians of the importance of modern science in industrial competitiveness, or a decision that science is a low-priority national issue, or worse still, both.

Linking Research Outcomes to Socioeconomic Progress

It cannot be assumed that greater public awareness of S&T will necessarily promote public support for research (*9*). The potential to apply genetics research to improve human health will be influenced as much by the social environment in which scientific advances occur, and in which they are to be applied, as by research progress per se (*10*). Enabling the public at large to participate in the debate on S&T goals will remain a major challenge as citizens become increasingly cocooned from risk, expecting simple answers to complex problems and obtaining information from sensationalist media accounts that promise instant breakthroughs or impending catastrophe.

The economic and social dislocations created by new technologies can also pose troubling problems for all governments. New technology may create unemployment in

R. Fears is Director of Science Policy and G. Poste is Chairman of R&D, SmithKline Beecham Pharmaceuticals, New Frontiers Science Park, Harlow, Essex CM19 5AW, UK.
M. W. J. Ferguson is Professor and Dean of biological sciences, University of Manchester, Manchester M13 9PT, UK.
W. Stewart is President of The BioIndustry Association, Belgrave Square, London SW1X 8PS, UK.