

References and Notes

1. *Facts and Figures* (American Cancer Society, Washington, D.C., 1977).
2. V. T. DeVita, Jr., V. T. Oliverio, F. M. Muggia, P. W. Wiernik, J. Ziegler, A. Goldin, D. Rubin, J. Henney, S. Schepartz, *Cancer Clin. Trials* **2**, 195 (1979).
3. L. S. Goodman *et al.*, *J. Am. Med. Assoc.* **132**, 126 (1946).
4. S. Farber, L. K. Diamond, R. D. Mercer, R. F. Sylvester, J. A. Wolff, *N. Engl. J. Med.* **238**, 787 (1948).
5. R. Li, R. Hertz, D. B. Spencer, *Proc. Soc. Exp. Biol. Med.* **93**, 361 (1956).
6. C. G. Little, *Carnegie Inst. Washington Publ. No. 179* (1913), p. 17.
7. G. G. Zubrod, S. Schepartz, J. Leiter, *Cancer Chemother. Rep.* **50**, 349 (1966).
8. V. T. DeVita, V. T. Oliverio, F. M. Muggia, P. W. Wiernik, J. Ziegler, A. Goldin, D. Rubin, J. Henney, S. Schepartz, *Am. J. Clin. Oncol.* **2**, 216 (1979).
9. P. Calabresi and R. E. Parks, Jr., in *The Pharmacological Basis of Therapeutics*, A. G. Goodman and A. F. Gilman, Eds. (Macmillan, New York, ed. 6, 1980), p. 1256.
10. G. B. Elion and G. H. Hitchings, *Adv. Chemother.* **2**, 91 (1965).
11. G. Heidelberger, in *Cancer Medicine*, J. F. Holland and E. Frei III, Eds. (Lea & Febiger, New York, ed. 2, 1982), p. 801.
12. T. Kalman, *Drug Dev. Res.* **1**, 311 (1981).
13. B. Rosenberg, L. VanCamp, J. E. Trosko, V. H. Mansour, *Nature (London)* **222**, 285 (1969).
14. S. A. Waksman and H. B. Woodruff, *Proc. Soc. Exp. Biol. Med.* **45**, 609 (1940).
15. A. Di Marco, in *Cancer Medicine*, J. F. Holland and E. Frei III, Eds. (Lea & Febiger, New York, ed. 2, 1982), p. 872.
16. H. Umezawa, in *ibid.*, p. 860.
17. I. S. Johnson, in *ibid.*, p. 910.
18. R. W. Ruddon, *Cancer Biology* (Oxford Univ. Press, New York, 1981), p. 330.
19. A. Gellhorn and E. Hirschberg, *Cancer Res. Suppl.* **3**, 1 (1955).
20. L. W. Law, *Nature (London)* **169**, 628 (1952).
21. S. E. Salmon, A. W. Hamburger, B. Soehnlen, B. G. M. Durie, D. S. Alberts, T. E. Moon, *N. Engl. J. Med.* **298**, 1321 (1978).
22. V. T. DeVita, *J. Natl. Cancer Inst.* **2**, 195 (1979).
23. E. J. Freireich, E. Gehan, D. Rall, H. E. Skipper, *Cancer Chemother. Rep.* **50**, 219 (1966).
24. V. T. DeVita, Jr., S. Hellman, S. A. Rosenberg, *Cancer: Principles and Practice of Oncology* (Lippincott, Philadelphia, 1982), p. 198.
25. E. Frei III, V. T. DeVita, Jr., J. H. Moxley III, P. P. Carbone, *Cancer Res.* **26**, 1284 (1966).
26. L. H. Einhorn, *Testicular Tumors* (Masson, New York, 1980).
27. Revised Regulations on HHS Policy for the Protection of Human Research Subjects, *Fed. Regist.* **46**, 8366 (1981).
28. G. G. Zubrod *et al.*, *J. Chronic Dis.* **11**, 7 (1960).
29. H. E. Skipper, F. M. Schabel, W. S. Wilcox, *Cancer Chemother. Rep.* **35**, 1 (1964).
30. E. Frei III *et al.*, *Blood* **37**, 272 (1971).
31. E. J. Freireich, E. S. Henderson, M. R. Karon, E. Frei III, in *The Proliferation and Spread of Neoplastic Cells* (Williams & Wilkins, Baltimore, 1968), p. 441.
32. E. Frei III, *Cancer Res.* **32**, 2593 (1972).
33. R. J. A. Aur, J. Simone, H. O. Hustu, T. Walters, L. Borella, C. Pratt, D. Pinkel, *Blood* **37**, 272 (1971).
34. V. T. DeVita, Jr., A. Serpick, P. P. Carbone, *Ann. Int. Med.* **73**, 881 (1970).
35. ———, *N. Engl. J. Med.* **298**, 907 (1978).
36. A. Goldin, J. M. Venditti, S. R. Humphreys, N. Mantel, *Science* **123**, 840 (1956).
37. D. S. Martin, R. A. Fugmann, P. Hayworth, *J. Natl. Cancer Inst.* **29**, 817 (1962).
38. M. Perloff, J. F. Holland, E. Frei III, in *Cancer Medicine*, J. F. Holland and E. Frei III, Eds. (Lea & Febiger, New York, 1982), p. 515.
39. S. Farber, B. Toch, E. M. Sears, D. Pinkel, *Adv. Cancer Res.* **4**, 1 (1956).
40. B. Fisher *et al.*, *N. Engl. J. Med.* **292**, 117 (1975).
41. G. Bonadonna *et al.*, *Sem. Oncol.* **5**, 450 (1978).
42. S. E. Salmon and S. E. Jones, Eds., *Adjuvant Therapy of Cancer* (Grune & Stratton, New York, 1981), vol. 3, p. 305.
43. V. T. DeVita, Jr., J. E. Henney, S. M. Hubbard, in *Cancer: Achievements, Challenges, and Prospects for the 1980's*, J. Burchenal and H. Oettgen, Eds. (Grune & Stratton, New York, 1980), p. 859.
44. L. M. Axtell, personal communication; F. P. Li, R. R. Connelly, M. Myers, *J. Am. Med. Assoc.* **247**, 825 (1982).
45. V. T. DeVita, Jr., in *Adjuvant Therapy of Cancer*, S. E. Salmon and S. E. Jones, Eds. (Grune & Stratton, New York, 1981), vol. 3, p. 3.
46. J. Holland and E. Frei III, Eds., *Cancer Medicine* (Lea & Febiger, New York, 1982), p. 627.
47. S. E. Sallan, N. E. Zinberg, E. Frei III, *N. Engl. J. Med.* **293**, 795 (1975).
48. D. L. Longo, *Ann. Int. Med.* **95**, 352 (1981).
49. V. T. DeVita, Jr., *Cancer* **47**, 1 (1981).
50. H. Suit, E. Hall, E. Frei III, *Am. J. Clin. Oncol.* **4**, 37 (1981).
51. J. H. Glick and S. G. Taylor, *Int. J. Radiat. Oncol. Biol. Phys.* **7**, 227 (1981).
52. J. C. Asquith, M. E. Watts, K. Patel, *Radiat. Res.* **60**, 108 (1974).
53. E. Frei III *et al.*, *Am. J. Med.* **68**, 370 (1980).
54. T. C. Merigan, Jr., K. Sikora, J. H. Bredeen, R. Levy, S. A. Rosenberg, *N. Engl. J. Med.* **229**, 1449 (1978).
55. K. Illmensee and B. Mintz, *Proc. Natl. Acad. Sci. U.S.A.* **73**, 549 (1976).
56. E. L. Reinherz and S. F. Schlossman, *Cell* **19**, 821 (1980).
57. T. A. Lister, M. M. Roberts, R. L. Brearley, R. K. Woodruff, M. F. Greaves, *Cancer Immunol. Immunother.* **6**, 227 (1979).
58. V. Raso and T. Griffin, *Cancer Res.* **41**, 2073 (1981).
59. T. G. Krontiris and G. Cooper, *Proc. Natl. Acad. Sci. U.S.A.* **78**, 1181 (1981).

The Role of Science in a New Era of Competition

George A. Keyworth, II

Anxiety runs high in Washington when there is a change in administration, and the delay in my arrival as science advisor no doubt contributed to the uncertainty last year about the role of science and technology in the Reagan Administration. The first formal presentation of the new Administration's science policy was made in June 1981 at the sixth annual AAAS Colloquium on R & D and Public Policy. That presentation of the broad context for science and technology policy was an event that I enjoyed thoroughly—until I started reading in the press

what it was I had supposedly said and what it supposedly meant. Now, a year later and a bit wiser, we owe it to ourselves to look realistically at the situation and opportunities at hand.

I would like to look beyond the immediate topic of the research and development budget for fiscal year 1983. Instead, I want to offer some thoughts about how science and technology fit into this Administration's goals for the country and share some ideas on what role we, the science community, must play in coming years.

No conference on federal R & D priorities can ignore the overriding significance of our country's economic condition. It is the dominant factor in virtually all deliberations on policy issues at the

White House. Not only does the economy determine how much R & D the nation can pay for, but it also influences what kind of R & D we will do. As I will discuss, R & D are important to our immediate economic recovery and critical to our long-term health—and the President is well aware of that.

Controlling Federal Spending

The President has been attacking the nation's economic problems directly through a combination of fiscal policies. In spite of all the public hand-wringing, I am convinced that most people recognize the inescapable truth of what must be done to restore America's luster. And in June the Congress made some hard political choices and finally approved a responsible federal budget for fiscal year 1983.

It is clear that economically this has not been a good year for the United States. For nearly two decades we have been living increasingly beyond our means—or neglecting to replenish our means to keep pace with our aspirations—and it is finally taking a brutal toll. High inflation, higher taxes, and crippling interest rates have been eroding our ability and incentive to prepare for the future.

The author is science advisor to President Reagan and director of the Office of Science and Technology Policy, Executive Office of the President, Washington, D.C. 20500. This article is adapted from his speech to the AAAS Colloquium on R & D and Public Policy on 23 June 1982.

A whole generation in our society has literally grown up with generous government programs. To them, reductions in the rate of growth in federal spending must seem positively un-American, and actual cutbacks are almost unthinkable. Unfortunately, cutbacks have to be part of the solution to restoring health to our economy.

Obviously, controls on federal spending are having broad and painful effects on federal programs. For that reason the modest, but real, growth slated for R & D and for basic research in the fiscal 1983 budget is highly significant and noteworthy. But, surprisingly, these increases have been ignored by many in the scientific community.

This puzzling response strikes me as analogous to a situation that I encountered before I came to Washington. I remember a theoretical nuclear physicist who had devised a comprehensive theory of nuclear isomers. His theory was increasingly assailed and challenged, and in due course a final experimental finding was inconsistent with his theory. His classic response to that finding was, "I like my theory. Don't encumber it with facts."

Likewise, I am afraid much of the science community in the past year has been obsessed with some kind of theory that the Reagan Administration was out to cut science budgets for various ideological reasons. So pervasive was this belief that the actual increase proposed for R & D, the second largest increase of any budget function, went virtually unnoticed. Instead of recognizing the importance placed on R & D in the budget, especially in comparison to other federal programs, the science community, like that physicist, did not want to be encumbered with facts.

Restructuring Priorities

Let me offer just two examples of these kinds of reactions to funding decisions. For 10 years support for the three major Department of Energy (DOE) high energy physics facilities—Stanford Linear Accelerator Center, Fermi National Accelerator Laboratory, and Brookhaven National Laboratory—has been falling behind inflation. Today they are starved into a state of near intellectual malnutrition. To address this situation, I posed the following question to the High Energy Physics Advisory Panel, appointed by both DOE and the National Science Foundation: "What would be necessary to maintain the leadership of the United States in high energy physics

through this decade and beyond?" Following their advice, we added nearly 20 percent to the DOE high energy physics budget to ensure optimal use of existing facilities and the ability to meet future demands for new experimental facilities. This was accomplished in the midst of severe fiscal constraints.

Nevertheless, the reports of this action addressed the demise of a facility—the Isabelle accelerator at Brookhaven—to which the high energy physics community would attach high priority only if a 35 percent increase in the budget could be implemented.

The Administration also proposed nearly a 20 percent increase in the budget for space science research because we saw tremendous opportunities for a broad research program with the space shuttle. We emphasized the astrophysics and astronomy research programs available with the shuttle, including the Space Telescope. At the same time, we asked the planetary science community to restructure their program to provide more missions at lower cost. After all, the cost of each mission was approaching \$1 billion, which was equal to the annual budget of the National Science Foundation. Our objective was to sustain a vital but realistic effort in planetary research. Yet to hear the space science community, we have gutted their activities.

I am reluctant to conclude that the science community, which I hold in high regard, is unable to rise above the kind of thinking that assumes that once started a program must not only continue, but grow, independent of scientific priorities. That kind of attitude is too prevalent. Recently, among a group of politicians who were addressing the role of science and technology in our future, I heard a senator attack the Administration for reducing funds for windmill research as an example of how we were cutting basic research. Faced with responses like these, how can we take those fresh looks at research priorities that scientists routinely do when new opportunities for more promising research come along?

The Role of the Federal Government

It is important that we not let intramural squabbles about shifts in research priorities overshadow a far more important aspect of science policy. Last year this Administration explicitly stated our intention of moving the federal government out of the areas of development and commercial demonstration activities, except where the government was

the customer. At the same time, we emphasized the federal government's strong commitment to ensuring a healthy, stable research enterprise. Our aim was to make a clear-cut and predictable distinction between what should be public sector and what should be private sector responsibilities.

We had two goals in mind. The first was to achieve what we believe is the properly limited role for the federal government as well as one that makes sense for a free-enterprise economy. The second was to give some clear signals to the private sector, which has to make investment decisions based on some assurances of what markets will look like in the future. There is nothing like the hint of the government stepping in to an area of research to effectively dissuade private companies from putting their own money into it.

In general, we wanted to strengthen the government in vital activities that it does well, such as basic research, and get it out of those it does poorly, such as demonstrating commercial technologies. Perhaps the latest noteworthy example of a misplaced government priority has been our support for demonstration projects in fossil and solar energy. We spent \$30 billion in pursuit of programs that had no significant likelihood of helping achieve the energy independence to which they were supposed to contribute. Why did they fail? Because there was no natural market for the products of those expensive technologies. It is no wonder that private industry was reticent to invest large amounts of its own money to improve the technologies.

What made the government plunge into such ill-fated activities? There were a number of political and social reasons, but to my mind they were all predicated on the wishful thinking that government could somehow operate independent of market forces—that it could subsidize a technology into competitiveness. In keeping with our policy for science and technology, we are pulling back now, removing government from demonstration projects that would be well within the capability of private industry to make competitive, if there is a market. At the same time we are concentrating, and at lower cost, on pursuing the kinds of research that may lead to true technological breakthroughs in energy.

This brief description of the major philosophical elements of our science policy is not new, but I did want to present some specific examples of how this philosophy guided us in putting together the proposed budget for fiscal 1983.

Competition from Abroad

Let me turn now to what I see as an important part of today's science and technology issues. In thinking about R & D we have to consider more than what kinds of science and technology we can afford in today's economy. It is more important to consider the reverse. How can science and technology help the economy?

I think the case can be made that the weak economy we inherited is at least in part the result of what I would call poor or even irresponsible fiscal management—primarily based on the idea that we could afford any popular federal program we wanted simply by printing more money. The ensuing economic chaos of inflation and high interest rates caused a serious secondary effect: caution and extreme preoccupation by business with the short term.

This secondary effect, in combination with some structural problems, has led to serious declines in the rate of productivity growth in many of our manufacturing industries. Not very many years ago these industries were the shining example of American inventiveness and technological wizardry. Today we find one industry after another threatened by strong competition from other countries, notably Japan.

We have already seen some large industries, such as steel and automobiles, severely battered by the competition. I do not want to overreact to the situation because, although our balance of payments in manufactured goods has deteriorated, it is still positive. But we already face a serious problem in the loss of American jobs, and even more important than the loss is our inability to replace them with other jobs. We should remember that this country, which has a successful history of moving up the technological scale and increasing labor productivity, expects to slough off jobs in aging industries because it can use people better in new industries.

The ironic thing is that some of our technological industries are losing out to foreign competitors in spite of the existence, in the United States, of the best basic research establishment in the world. Our better universities remain the world's best, and our graduate schools are imitated but never equaled. More than 300,000 foreign students attend American universities today; they know how good our schools are.

My first reaction to this situation is that, despite what the economists say, there is no guaranteed relation between

the money spent on R & D and national economic growth. I am not suggesting that we can have economic growth without R & D, but R & D is obviously not in itself sufficient. Japan is a fascinating example because it spends relatively little on basic research but has been successful in a way that we have not. The Japanese have put knowledge to work. Often it is knowledge from research efforts here that they have put to work, but any of us who have worked in basic research know that the transfer process does not respect national boundaries. The best protection against this kind of information drain is not protectionism; it is for us to be as aggressive in applying knowledge as we are about pursuing it.

The Japanese Dilemma

We know by now that Japan does some things very well, but we should not be carried away in our adulation for that particular economic and social system. We look at Japanese manufacturing and wonder how we might achieve the same kinds of process efficiencies and worker productivity gains. But the Japanese themselves are increasingly concerned about their own future because they lack the very strengths that we have in abundance—creativity and flexibility. According to Steve Lohr in a recent *New York Times* article (13 June 1982, section 3, p. 1), the traits that brought so much success to Japan's carefully planned and integrated industries now threaten the country's industrial future.

The article points out three budding problems. First, the Japanese system of management, which is seniority-based, is often ill-suited to fast-moving, emerging markets. Second, their system of corporate financing thwarts the start-up of new, innovative industries. Third, and I quote Lohr, "the country's emphasis on community, obedience, and uniformity, all of which have been crucial to its highly efficient assembly lines, has discouraged individual creativity and, with it, far-reaching product inventions."

Japanese leaders now see ominous signs; they may face problems in continuing their whirlwind success in building new industries that capitalize on emerging technologies. In many ways Japan has been able to operate with far lower overhead than we have in the United States. Japan spends far less than we do on defense, on social programs, and on basic research and has been able to allocate more of its resources to indus-

trialization. But problems are beginning to emerge. Japan's celebrated worker security system, for example, is partly possible because the population is young, with more than twice as many people working per retiree as in the United States and Western Europe. But since 1949 life expectancy in Japan has jumped from 55 to 76 years; in less than 20 years Japan, too, will be carrying social support costs for retired workers that are comparable to ours.

Moreover, it seems that Japanese leaders are also worried about their relative inattention over the years to basic research and to the encouragement of creativity in general. Just as the United States was able to make phenomenal strides in technology during the war years because of the backlog of basic science that had accumulated during the 1920's and 1930's, Japan may have been able to make its rapid industrial advances in the 1960's and 1970's by tapping into a mother lode of new production and manufacturing opportunities that have now been substantially used up. Its high-volume, carefully balanced industrial system is fragile and highly susceptible to shifts in technologies and in markets. How well it will continue to flourish without fresh creative input is an interesting question. I am not at all sure that we should be envious of Japanese industrial methodology, and we certainly should not try to slavishly copy it.

The Future of U.S. Technology

What we should be doing is capitalizing on our own substantial advantages and letting the creativity of our science enterprise light the way for new industrial innovation and development. There is no question that our future, as a nation, is tied to high technology. That is where the jobs will be, and that is where the driving force in international trade will be. Even our premiere industry—agriculture—may be on the verge of a new revolution because of developing high technology.

Unfortunately, we have failed over the years to take full advantage of our own resources. Researchers in universities, in federal laboratories, and in industry have tended separately to pursue their own interests and have even developed their own internal communication networks. Sometimes I am not even sure that the different scientists and engineers speak the same language. In the short run this inefficiency most hurts industry, which is impeded in capturing new ideas

that might have commercial potential. In the long run, of course, we all suffer if our industries cannot compete in the international market.

We know that, as a great industrial nation, we have made some serious blunders in recent years. Mostly I think our mistake was in taking our industrial superiority for granted. We assumed that our lead was insurmountable and that upstart economies would, at best, carve out some small market niches that we did not want to bother with because we assumed that the profit was low—small cars are an example—or that they would take over some undesirable, labor-intensive manufacturing that Americans had outgrown. We are finally beginning to recognize the seriousness of our situation, and we are in an excellent position to do something about it.

Admittedly it would be easier to mobilize the nation's resources into a new technological express in the face of something comparable to the challenge of a Sputnik. Still, I think by now most people would agree that the threat of industrial decline and the inability to compete with other countries is a serious threat. I am suggesting that just as we demonstrated our national capacity to achieve greatness with the space program in the 1960's, we should mobilize ourselves for a comparable surge in industrial strength in the 1980's.

How can we make that surge possible? One way will certainly be to establish closer ties between the people putting science and technology to work and those in basic research. We have already introduced measures to encourage industry to support some research in the universities. Now this is not simply a matter of industries "buying" research from the campus; the process involves a sharing of ideas and of people. At the same time that university researchers are getting a better understanding of industrial goals, industry should be able to offer university faculty a chance to participate in new kinds of research and to take advantage

of environments that are not likely to be found on the campus.

I am not suggesting that industrial funds are ever going to take the place of federal funds for university basic research. The federal government recognizes its responsibility and self-interest in maintaining a strong basic research capability. But as one who has to answer to the questions of what kinds of returns the taxpayers get on the billions of dollars spent each year on basic research, I am certainly anxious to help establish mechanisms that will improve the likelihood that knowledge will be transformed into public benefit.

It is encouraging to see the apparent reawakening of interest on the part of businesses in making the kinds of long-term investments in R & D that can transform industries. Improvement in the economy, which is the President's highest priority, is likely to stimulate industrial R & D as individual firms position themselves for highly competitive future markets. There is going to be an extremely active and intellectually stimulating interface developing between some universities and some industries. We are already seeing examples of this in biotechnology. Institutions that identify appropriate opportunities and devise working arrangements will find themselves immersed in what promises to be mainstream areas of science and technology activity for the rest of this decade—and probably for the rest of the century. They will have better opportunities to attract additional support for campus research, and they will be able to attract and retain faculty who find industrial laboratories stimulating and well-equipped places to do research.

Universities cannot order up a boom in high school students to reverse the reality of declining college enrollments, nor can they stop young men and women from wanting to be engineers or stop engineers from wanting to work for industry rather than for universities. But contained within new institutional ar-

rangements are likely to be creative approaches to the nagging problem of providing innovative employment and research opportunities for young faculty, to problems of inadequate on-campus instrumentation, and even to shortages of faculty in fields with high industrial interest.

The United States is undergoing substantial change. Although political policies may shift the timetable a little in one direction or another, it was inevitable that sooner or later we would have to face up to the rise of highly competitive industrialism among other ambitious nations. These are definitely not challenges to be taken lightly, but there is every reason for us to take them on boldly. Scientists and engineers must be the boldest of all.

As schoolchildren we were taught that the phenomenal growth of the United States as an industrial nation was primarily a product of abundant raw materials and plentiful, cheap labor. That is not the whole of it. Embedded in our society even a century ago were two more important driving forces: a free-enterprise system that thrived on innovation and invention and a form of society that encouraged and admired independent thinking and creativity.

The Reagan Administration is committed to maintaining the world's strongest scientific and technological base. At the same time, a new spirit of innovation must rise from within the scientific and technological communities. Merely to fall back on the patterns of reaction to our last great technological challenge, Sputnik, is not an adequate approach to meet today's challenges. We in the scientific and technological communities must respond with new vigor and new vision. I have no doubt that we can do so; we must first recognize, however, the unique elements of today's challenges and devise new, creative mechanisms to address them. It will not be easy, but the lessons of the past year convince me that we can do it.