COMMENTARY

by Bernard Dixon

LESSONS FOR MEDDLERS

Next month marks one decade since that historic Gordon Research Conference following which Maxine Singer and Dieter Sol, the two cochairmen, wrote to the president of the National Academy of Sciences regarding the newly developed "ability to join together, covalently, DNA molecules from diverse sources." Outlining possible benefits from this technique, they also expressed disquiet about theoretical hazards to laboratory workers and the public from novel organisms spawned as a result of such a biologically unprecedented procedure. Publicized through the columns of *Science* (**181:** 1114), that letter triggered off the furor which led to the Asilomar conference in February 1975. There followed an acrimonious public debate concerning scary monsters, and an acrimonious professional debate over prudent regulations for recombinant DNA manipulations.

Ten years later, with guidelines relaxed and those hypothetical dangers having been dismissed as unreal or unimportant, there is a tendency to see the entire controversy as a storm in a teacup. Some scientists who played a major role in ventilating honest apprehensions now feel they went too far, attracting grotesquely ill-informed political opposition and diverting their energies away from the laboratory bench and towards committee rooms and public platforms. Given the opportunity, next time around they would probably decide not to blow the whistle.

If such (understandable) weariness were to make today's biotechnologists underrate political and public concerns, the results could be calamitous. Logic is far from being the only motive force behind scientific and commercial development. British Petroleum discovered that truth some years ago when a combination of post-Seveso environmental sensitivity and pressure from the soybean lobby persuaded the Italian government to ban BP from operating its single-cell protein plant in Sardinia. The company eventually pulled out of microbial food altogether. Total cost: £100 million.

But what of rationality and irrationality about gene splicing today? On the side of sanity, we have a long catalogue of reassurance: the mediocrity of *Escherichia coli* K-12 as an Andromeda strain, the development of totally safe hosts for recombinant DNA work, the presence of introns in eukaryotic genes which thus cannot be expressed in prokaryotes, the dismal failure of simulated disasters such as animal infection with *E. coli* containing polyoma genes, and Stanley Cohen's work showing that DNA maneuvers of the sort which caused Erwin Chargaff and fellow critics such anxiety are not as radically new as was thought.

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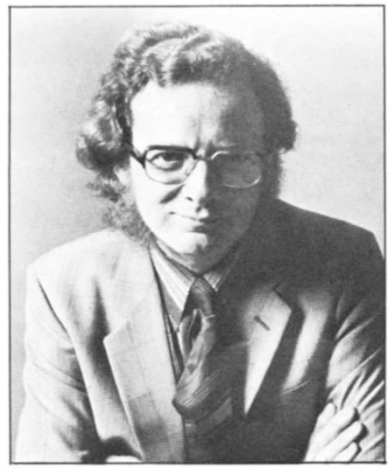
There is another, broader argument. Any critical extraterrestrial monitoring our affairs would surely be astonished by the contrast between intense, recent concern over manipulations conducted under conditions of cast-iron containment, and the manifold ways in which we have modified terrestrial genomes during centuries past. In their recent, thought-provoking book *Genetic Consequences of Man Made Change* (Academic Press), J. A. Bishop and L. M. Cook show just how drastic such changes, conscious and otherwise, have been. Consider, for example, the monoculture of astronomical areas of genetically identical plants which characterizes modern agriculture. Think of the proliferation of heavy metal-resistant species caused by the dumping of mining wastes on the earth's surface, and other toxic materials in the environment.

Above all, there is the appalling spread of bacterial drug resistance produced by uncontrolled, indiscriminate use of antibiotics. As Stuart Levy observed recently in *The Lancet* (1982, **2:** 83), this now poses a serious threat to public health throughout the world. Looking back, it is difficult to disagree with the sentiments of the bacteriologist E. S. Anderson—expressed early on in the past decade's debate—that such feckless disregard for the ill-consequences of antibiotic misuse was infinitely more dangerous than any risks arising from recombinant DNA work done in high security facilities.

Evidence for the safety of a new technology, plus favorable comparisons with thoughtless follies elsewhere, does not, however, constitute a case for boundless buoyancy. On the one hand, as Ditta Bertels and colleagues pointed out recently (*Trends in Biochemical Sciences,* 1983, **8:** 78), some of the reassuring evidence that led to the relaxation of guidelines is itself being reassessed. Thus, they argue, the discovery of processed genes without introns in higher animals resurrects one of those earlier anxieties. "During the intervening period of four years most of the stringency conditions which were initially incorporated in various local and national guidelines have been scrapped," they write. "Until more is known about the expression of cloned processed genes in bacteria, uncertainty about the biohazard of cloning animal DNA will remain."



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So much for the intellectual case. Equally significant for those scientists and administrators involved in biotechnology is the need for caution in a wider sense. Just one accident during "scale-up," for example, could forfeit public confidence and set back R&D spectacularly. Similarly, just one mischievous television program might easily renew and reinforce the very worst fears about what Chargaff once called "genetic meddling."

In considering such possibilities, we would be wise to bear in mind the capricious, as well as substantive, factors which held to propel ideas into the

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public arena and make them fashionable concerns. Who, for example, would have foreseen that, after being overshadowed by nuclear power for a decade or more, nuclear weaponry would suddenly again become a major political issue in the Western world? Who would have prophesied the emergence of animal experimentation as a passionate talking-point in Europe? How to account for the furor surrounding the world's first round of heart transplants in the late 1960s, compared with the conspicuous lack of public interest about the more recent second round?

As BP found at great cost in Sardinia, it is at least as important to grapple with social and political ramifications as it is to get the science and technology right. Perhaps (in addition to the ecologist I suggested recently) every company investing in biotechnology should have a first-rate sociologist on board. Or even a clairvoyant . .