SCIENTIFIC COMMUNITY

Asilomar Revisited: Lessons for Today?

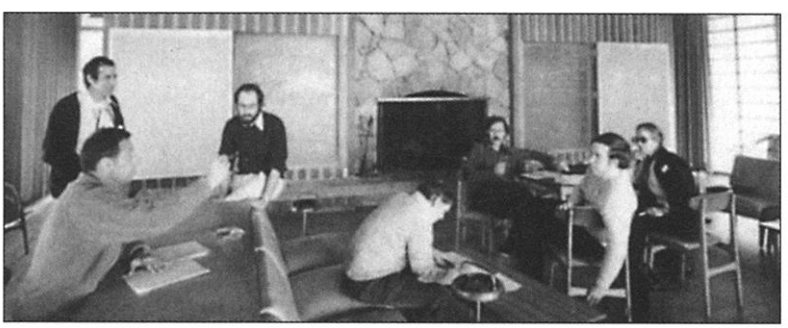
A conference last month asked whether the "Asilomar process" could help to resolve today's biotech controversies

PACIFIC GROVE, CALIFORNIA—The Asilomar conference on recombinant DNA was the Woodstock of molecular biology: a defining moment for a generation, an unforgettable experience, a milestone in the history of science and society. But was it something that could—or even should—be repeated?

Those were some of the questions on the minds of 55 scientists, lawyers, historians, and ethicists who gathered here last month at the Asilomar Conference Center near Monterey to mark the 25th anniversary of that historic meeting. In February 1975, 140 participants—mostly biologists, with a handful of lawyers and physicians and 16 members of the press—gathered at the rustic conference center overlooking the Pacific to tussle with an issue that had just burst onto the biology scene: the safety of recombinant DNA research. Known officially as the International Congress on Recombinant DNA Molecules but remembered ever since simply as "Asilomar," that meeting was widely hailed as a landmark of social responsibility and self-governance by scientists. The participants in last month's conference*—who included 11 of the 1975 conferees—were not just here to reminisce. Legal scholar Alex Capron, a participant in the 1975 meeting and now co-director of the Pacific Center for Health Policy and Ethics at the University of Southern California in Los Angeles, assembled the group to discuss what lessons could be learned from the "Asilomar process" and, specifically, whether there are situations today in which it might be appropriately applied.

Asilomar occurred at a unique moment in biology. Researchers had just discovered how to cut and splice together the DNA of disparate species and were beginning to contemplate the cornucopia of experiments this opened up. "Recombinant DNA was the most monumental power ever handed to us," said California Institute of Technology president David Baltimore, one of the organizers of the 1975 meeting. "The moment you heard you could do this, the imagination went wild." But a number of scientists at the time raised concerns about whether such experiments might create dangerous new organisms, microscopic Frankensteins that could sneak out of the lab undetected on the sole of a Hush Puppy and threaten public health.

Those concerns triggered a "hectic experience" of scientific soul-searching that culminated in the 1975 Asilomar conference, recalled Stanford molecular biologist Paul Berg, another organizer of that meeting. Participants at a June 1973 Gordon Conference on Nucleic Acids had published a letter expressing concern about recombinant DNA research. In response, Berg led a committee of the National Academy of Sciences that in July 1974 took the unusual move of calling for a voluntary moratorium on certain types of recombinant DNA experiments until the hazards could be evaluated.



1975 Asilomar participants. Left to right, Norton Zinder (standing), Paul Berg (seated, foreground), David Baltimore, Sydney Brenner, Richard Novick, Richard Roblin, and Maxine Singer.

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Berg and several colleagues organized the Asilomar meeting 7 months later to bring together "people who were engaged in the research or were likely or eager to use it." The organizers also brought in researchers with expertise in bacteria and viruses to help assess the potential hazards. A sense of urgency pervaded the meeting, in part because researchers were impatient to put the new technology to work. Although most of the participants suspected that there was no real hazard, Baltimore said, the stakes were clearly "too important to be wrong." The meeting's organizers decided not to address the ethical issues surrounding genetic alteration but to stick to safety issues they felt they could address as scientists. After much haggling, the group settled on a set of safety guidelines that involved working with disabled bacteria that could not survive outside the lab. The guidelines not only allowed the research to resume but also helped persuade Congress that legislative restrictions were not needed—that scientists could govern themselves.

The group that convened last month faced a very different set of circumstances. The technology that seemed like science fiction in 1975 is now commonplace and has yielded what Baltimore called "a remarkable harvest" of products and applications, such as genetically enhanced crops, tests for genetic diseases, and human gene therapy. Last month's meeting also had less of a sense of urgency because, for the most part, scientists consider these technologies safe.

But the public remains hugely concerned about the applications of genetic manipulation: Witness the recent protests in Europe over genetically modified crops. And society today is much more insistent on participating in the debate. "There are no important risks that scientists alone can assess," said Princeton University president Harold Shapiro, chair of the National Bioethics Advisory Commission. "Scientists can make a great contribution, but they can't decide alone."

What's more, the scientists themselves have changed. Those who gathered at Asilomar in 1975 represented a research community that was purely academic in its interests. Today, "there are few pure academics left" in molecular biology, Baltimore noted. As genetic engineering has gone commercial, academics have followed, and today most senior academic researchers have ties to biotechnology companies that would complicate any attempts at self-scrutiny.

During the course of last month's 2-day meeting, participants concluded that, for these and other reasons, it would not be appropriate now for scientists alone to take on the task of analyzing the risks of their work while setting aside the ethical issues, as they did a quarter-century ago at Asilomar. Nevertheless, as they debated the genetic modification of crops, gene therapy, and the use of genomic information, the participants identified instances in which society might have benefited if scientists had actively contributed to a

* Symposium on Science, Ethics, and Society: The 25th Anniversary of the Asilomar Conference, 15–17 February.

public debate about the safety of their work.

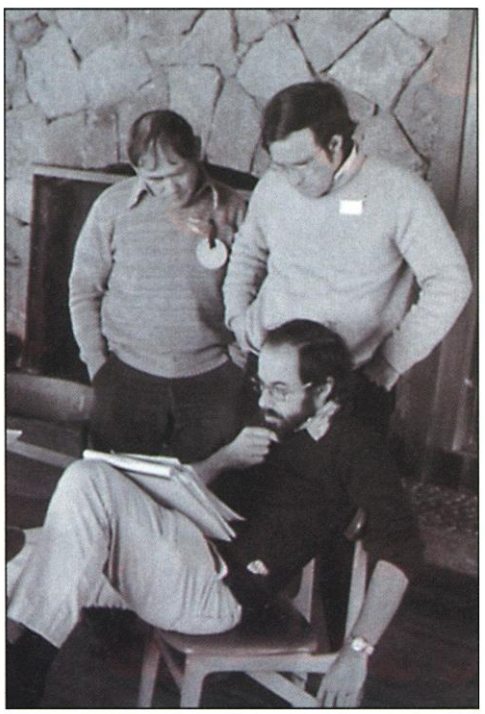
One of those was gene therapy, the subject of the most intense soul-searching at the meeting. Gene therapy has been in the hot seat since the death last September of Jesse Gelsinger, an 18-year-old subject in a gene-therapy trial at the University of Pennsylvania. Others in the field knew that the adenovirus vectors being used in the Pennsylvania trial could cause potentially dangerous immune reactions, like the one that apparently killed Gelsinger, said gene therapy researcher Inder Verma of the Salk Institute in La Jolla, California. "Why didn't we stand up" at meetings and raise those concerns? Verma asked.

Picking up on Verma's remark, Baltimore urged that "it is absolutely necessary" for gene therapists to slow down and reexamine the standards for when to begin trials on human subjects. "There are times when some things shouldn't happen," he said. Gene therapy vectors "that weren't working in animals are going into humans. A lot of us are saying what the hell are [doctors] doing putting these into people?" The Gelsinger death and the publicity it has generated are sure to raise public suspicion, said Maxine Singer, president of the Carnegie Institution of Washington: "It will be difficult to repair the damage that has already been done to biomedical research and gene therapy research."

Some participants also suggested that the huge public backlash against genetically engineered crops might have been averted if scientists, both commercial and academic, had taken a more active role in analyzing risks—not only as they perceived them but also as society was likely to—and perhaps exercised restraint until those uncertainties could be resolved. What made Asilomar unique was that the scientists "gave other people's perspectives some standing," said Shapiro. "Here is a case where commercial interests are suffering a great deal from not having confronted these problems in this way."

But with substantial U.S. acreage—for example, one-third of the corn and half of the cotton and soybeans—planted with genetically modified crops, it is too late to go back to a scientist-controlled process of self-regulation, said Rebecca Goldberg of New York City–based Environmental Defense. Indeed, it is naïve to think that any controversial issue can, or should, be resolved by scientists alone, said sociologist Dorothy Nelkin of New York University. She pointed out that public fears about the safety of new genetic technologies often mask deeper societal concerns. In the case of genetically modified crops, for example, "when the French talk about risk, they are talking about McDonald-ization of France and the plight of the small farmer. When the British talk about risk, they are worrying about the alteration of nature. Even if it could be demonstrated that the risks were acceptable, the controversy would continue."

Although it may be too late to influence the debate on genetically modified foods, at least some of the conferees thought an updated Asilomar-like analysis of scientific risks could still make an important contribution in two areas: germ line engineering and xenotransplantation. Gene therapy that alters germ line cells is an ethical minefield, as such alterations would be transmitted to future generations. "At Asilomar [in 1975], people said they would draw the line at germ line gene therapy," said science historian Charles Weiner of the Massachusetts Institute of Technology (MIT). Now, although germ line therapy in humans is not actually being done, "it's on the table" as an option, said Weiner. Weiner and others worry that techniques developed to correct genetic diseases may eventually be used to engineer desired traits into children.



Assessing risks. Brenner, Roblin, and Baltimore (seated) at the 1975 conference.

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In addition to those ethical concerns, the group debated scientific risks. Geneticist Arno Motulsky of the University of Washington, Seattle, argued that germ line therapy could "lead to reduction of genetic disease" and so should not be dismissed out of hand. But physician and geneticist Paul Billings, co-founder of GeneSage, a San Francisco Internet-based genetic information and health company, countered that germ line therapy is not necessary, given other options such as prenatal or preimplantation diagnosis of genetic defects. What's more, he said, the altered genes, especially if they insert randomly into the germ line genome, may have unpredictable and potentially very subtle negative effects on health or intelligence. Although difficult to detect, such effects could be "quite significant" to individuals and their descendents, said Billings. To MIT molecular biologist Phillip Sharp, debate such as this emphasizes the need for an Asilomar-like "attempt at evaluation and consensus in the scientific community" concerning germ line therapy.

As for xenotransplantation, the transfer of organs from nonhuman species into humans, there are concerns that the procedure could endanger public health by transferring animal viruses to humans. Other countries are considering or have instituted moratoria on the procedure, said Lana Skirboll, director of the Office of Science Policy at the U.S. National Institutes of Health, but the United States has done nothing. "We need a scientific assessment," she said.

At the end of last month's meeting, Berg reflected on the differences between 1975 and 2000 and what they might mean for the resolution of scientific controversies. One factor that made the first meeting work, he said, was the "suddenness of the issue." Because molecular biologists weren't yet heavily invested in recombinant DNA technology and the public knew little about it, "it was much easier to get people to agree on a course of action," Berg told *Science*. Most of the issues discussed at last month's conference are "chronic," he noted. And "once an issue becomes chronic, positions become hardened, and consensus is much more difficult to achieve." What's more, Berg and others noted that consensus might never have been reached if the scientists at Asilomar had not agreed to put aside the ethical issues and stick to biological hazards. In 1975, that process worked, and the research not only went on safely but won the public trust. Today "we are in a very different world," said philosopher Stephen Stich of Rutgers University in New Brunswick, New Jersey, where that public trust is not so easily won.

But that in no way diminishes the need for scientists to reflect on the impact of their work on society, said Susan Wolf, a professor of law and medicine at the University of Minnesota, Minneapolis. What was unique about Asilomar was that "a group of scientists was convened to reflect upon how their work affected other people's lives," said Princeton's Shapiro. And that, he and others agreed, is something that scientists owe society as they move toward whatever the next scientific revolutions might be. **–MARCIA BARINAGA**