THE PANDORA'S BOX CONGRESS

By Michael Rogers

140 Scientists Ask: Now that We Can Rewrite the Genetic Code, What Are We Going To Say?

The event was sufficiently historic that not until it was nearly over did anyone have time to think of taking a group portrait. And by then the official photographer had already departed and thus the International Conference on Recombinant DNA Molecules —a diverse mix of 140 scientists who manipulate the most fundamental life processes in laboratories from Moscow to Memphis—will remain pictorially unrepresented in the history of modern science.

But their activities, almost certainly, will not: The conference—four intense 12-hour days of deliberation on the ethics of genetic manipulation—should survive, in texts yet to be written, as both landmark and watershed in the evolution of social conscience in the scientific community.

And perhaps in the evolution of humanity itself.

"Nature," as a middle-European microbiologist told me late one night, "does not need to be legislated. But playing God does."

Abruptly, in a matter of months, the young science of molecular biology had happened upon the first real tools of genetic engineering: the ability to create, in the test tube, creatures never before seen on this planet. Thus far the technique was crude and extremely limited—but even so, the molecular biologists had clearly reached the edge of an experimental precipice that may ultimately prove equal to that faced by nuclear physicists in the years prior to the atomic bomb.

But in the last hectic hours before the conference slid, with the momentum of a base runner, into its conclusion, it would briefly appear that even those scientists with fingers on the most intimate genetic self-regulation processes of nature were themselves incapable of any similar scientific self-regulation.

The Arrival

"I can't room with you, man!" a middle-aged Scottish delegate in wool sports jacket exclaims to his newly assigned roommate at the Asilomar registration desk as, through broad picture windows, a crystalline orange Pacific sunset fills the sky above the white beach 200 yards to the west. The Scot, it appears, has just learned that his roommate, a young American, specializes in the lower mammals.

"I'm an invertebrate man, myself," the Scot explains, mock serious.

"Well," says the young American tentatively, somewhat taken aback. "Well," he admits slowly, "I'm an insomniac."

"Great!" says the Scot. "So am I. We can rewrite the proposal at three in the morning!" And then off they go, baggage laden, into the dusk and the van that carries attendees to the small redwood dormitories scattered throughout the wooded grounds.

The molecular biologists descend upon California's Monterey Peninsula on very nearly the same day as do the monarch butterflies. The Asilomar Conference Center, three hours south of San Francisco, is a scatter of rustic dormitories and spacious meeting halls, hidden in a seaside forest of redwood and Monterey pine, just outside the tiny town of Pacific Grove. Traditionally, each spring immense flocks of migrating monarchs, numbering in the millions, briefly cover the trees here in thick sheets of orange and black—an event of no small significance to the merchants of Pacific Grove.

This spring, along with the butterflies, come the biologists, arriving from everywhere and fueled by $100,000 put up jointly by two prestigious American organizations: the National Institutes of Health and the National Science Foundation. The conference was organized by the National Academy of Science.

They arrive on a bright blue Sunday afternoon—the finest February weather that the Monterey Peninsula has to offer—shuttled in from the local airport, often still clad in overcoats donned (hours earlier) in Cambridge or Kraków. Prominent on the Asilomar registration desk is a stack of mimeographed maps that detail the route one need follow to view the migrating monarchs but no one, this crisp Sunday, seems terribly interested in Lepidoptera.

"Yes!" a plump and bulkily sweatered New Yorker exclaims to a Japanese colleague. "We tried that; first you mutagenize the cell, then you cut. . . ." Sandwiched between pool and ping-pong tables, researchers meet for the first time in months, and even in the middle of an overwaxed linoleum floor, their discussions suggest both the vitality of small boys with new chemistry sets and the electricity of back yard gossip. The excitement is unmistakable. Clearly these people think they are *on* to something.

And the fact is, they are. And that, moreover, is precisely why they are at Asilomar.

It was, after all, only about a century ago that the Austrian monk Gregor Mendel, browsing in his monastery sweet-pea patch, first described the phenomenon of genetic inheritance. And far more recently that human beings identified the minute chemical container — deoxyribonucleic acid: the DNA molecule—in which that genetic information was actually stored.

That container — an intricate, lengthy, ladder-shaped organic molecule—holds the most widely understood language on the planet. The design of every living organism—from the paramecium in the mud puddle to Albert Einstein at Princeton—was at one point described in variations of precisely the same sinuous patterns. The most understood—and also the most difficult to translate. A single strand of human DNA, microscopically small, contains at least the information of a library of 1000 volumes.

The chemical keys to that library have been hard to find. To translate one volume, even harder. And to write one's own book—impossible.

Until recently. "Science," as a British biologist observed at Asilomar, "has built-in pauses; some last 100 years. But the thing about recombinant DNA engineering is that it's suddenly made many things very easy that were once very difficult." Recombinant DNA engineering is the reason for Asilomar: the discovery of the first rudiments of grammar for that previously unspeakable genetic tongue.

The ancient Greeks believed in a mythologic being called a Chimera—a female monster composed of pieces of two or more animals. Molecular biologists now believe in DNA molecules that they call precisely the same thing. Moreover, they make them themselves. Recombinant DNA engineering uses certain newly discovered enzymes to disassemble the long DNA molecule in so orderly a fashion that the loose bits of genetic coding may then be rejoined, grammatically, into coherent sentences. And such a sentence may well describe—and create—the mutual offspring of two altogether different creatures incapable of mating in nature. "To join duck DNA," as the same British biologist was fond of saying, "with orange DNA."

If one knows the grammar, one can begin to make up new sentences. Dial-a-baby, then? Or better, dial-a-monster? Not, by a long shot, yet. The brand-new techniques work, thus far, only with bacteria and viruses—organisms so small that human beings really only notice them when they make us ill.

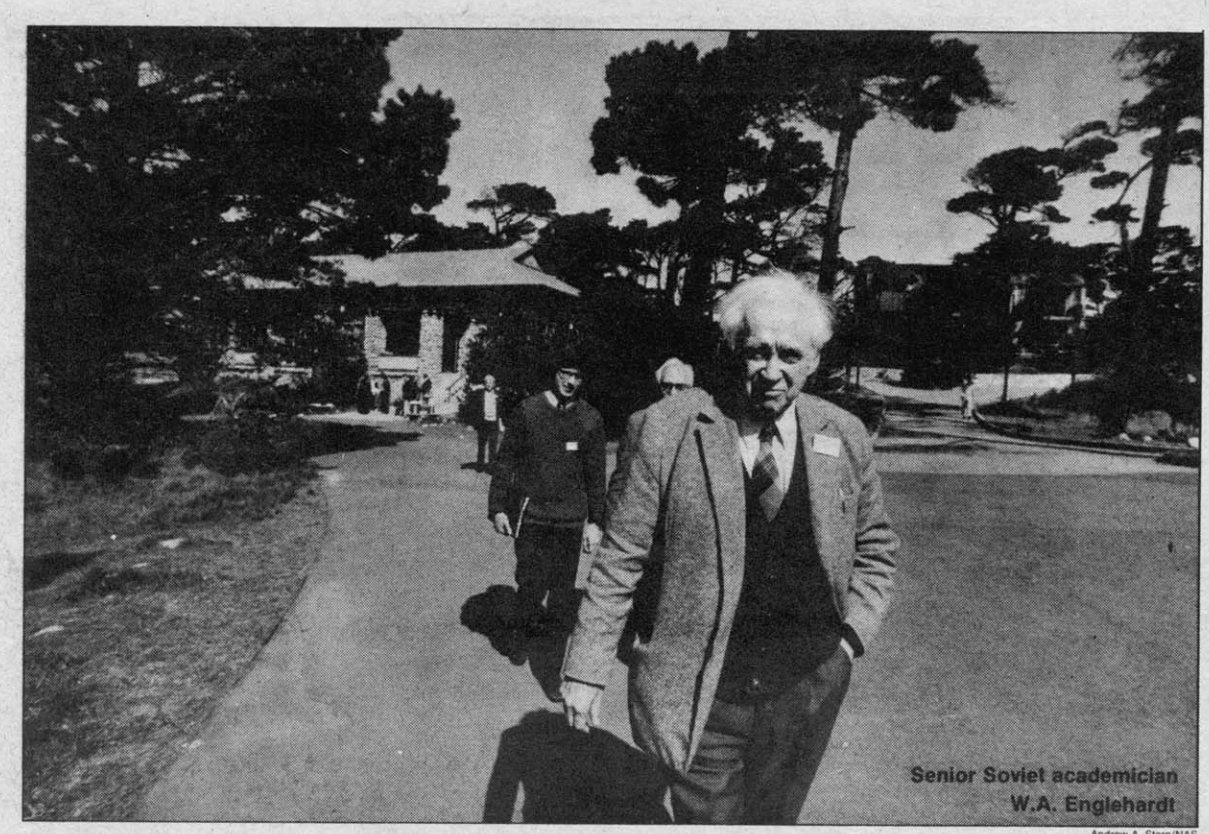
But there, precisely, lies the rub—and also fit meat for countless science fiction scenarios.

A Science Fiction Scenario

For starters, we'll cast a young molecular biologist who looks like Woody Allen, tends to shuffle a bit and mumbles, say, in the vaguely sullen fashion of a Cambridge-educated Stanley Kowalski. He should be exceedingly bright but not always terribly careful about laboratory hygiene.

He is most likely interested in cancer because cancer is where the money is just now, but he might just as well be curious about, say, the way bacteria learn to resist antibiotics.

The molecular biologist has several million laboratory helpers: a colleague or two, a couple of graduate students, a handful of technicians and an immense colony of bacteria called *Escherichia coli*—the last



Senior Soviet academician W.A. Englehardt

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of whom work only for room and board.

Those particular bacteria were recruited from a single human gut more than half a century before—and since then they have existed, almost exclusively, within the laboratory. A whole host of their relatives still reside quite happily in literally millions of human intestines — but since its isolation, this laboratory strain of K12 *E. coli*, as it is known to its friends, has had a far less placid existence.

In our scenario, the K12 *E. coli* is about to serve as something of a factory hand—an experimental workhorse — in a procedure called plasmid engineering.

A plasmid is a tiny circular bit of genetic information—DNA—that floats around inside the sack-like cell of a simple bacterium. Plasmids can affect the bacterium in some fairly significant ways; they are, for example, responsible for the increasing number of bacteria that are now learning resistance to old-line antibiotics like penicillin and tetracycline.

And here it is that our scenario really begins, for what our molecular biologist has set out to do is to produce plasmids of a variety never before seen in nature and then pump those novel plasmids into the patient old *E. coli*, whereupon *E. coli* will not only begin to obey the plasmid information but to reproduce it as well.

From here on, the scenario almost writes itself. The researcher, say, manages to isolate what he suspects to be a bit of the genetic information that causes tumor growth—an ability known technically as "oncogenicity." By grafting that bit of DNA onto a plasmid and introducing that modified plasmid into *E. coli*, he might just determine whether he has in fact identified those spurious genetic orders that cause normal cells to lose their biochemical minds.

If he has, and he follows up carefully, it could mean the Big Time; a major break in cancer research and—who knows?—the limelight, prizes, prestige, a funded research chair: all of the not inconsiderable gravy that can accrue to the very good or very lucky medical researcher in this country.

But this isn't a Cinderella scenario. So he gets sloppy; just once. Perhaps he has only recently turned to molecular biology from, say, chemistry and while he does his best, he still hasn't fully comprehended that his glassware now contains something far different from lifeless arrangements of molecules. Or perhaps a laboratory assistant is at fault, borrowing a page from an old story told about Fort Detrick—for years the highest-security center of American biologic warfare research—where an enlisted man, not so fresh from a weekend pass, once failed to seal securely a high-speed centrifuge and thus managed to spray the entire laboratory with a fine aerosol mist of concentrated and monstrously contagious plague.

At any rate, the long imprisoned *E. coli*, laden with a brand-new bit of biological ability, suddenly finds itself liberated; floating in a minute droplet on a technician's finger, then onto a tuna-fish sandwich and thence into a luckless human gut. Or, in a culture not quite completely killed, down some stainless steel laboratory sink and thus into a sewer system teeming with billions of close relatives.

And now what? Nothing to this point is excessively speculative: It was, after all, only two years ago that smallpox virus managed to escape from an experimental laboratory in London, killing two women in its characteristically swift—and incurable—fashion. So the really speculative part is yet to come: Precisely what could our artificially mutated *E. coli* do with its sudden freedom?

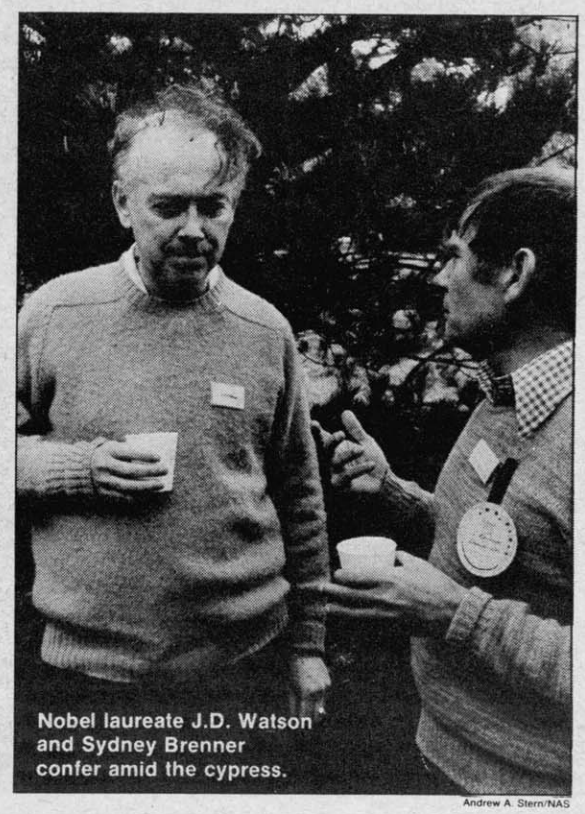
An epidemic cancer that spreads through the sewer system? A once conquered disease—like bubonic plague—now, abruptly, again incurable? Or a brand-new disease, sudden and mysterious, that has never before appeared in human beings?

At this point, there's no certain answer to the question. There is, simply, no further information on which to proceed—and there's no information precisely because the question deals with organisms that have never before existed on the planet. But the concern that brought 140 molecular biologists to Asilomar is clear: Human beings have once again happened upon the ability to threaten themselves with a blight that might someday prove to be the biological equivalent of nuclear radiation leakage.

But gamma rays, of course, cannot reproduce.

The Letter

"Eight months ago," says conference organizer Paul Berg late one afternoon at Asilomar, "the telephone calls were coming into our laboratory daily: 'Send us pSC101 [a variety of plasmid used for recombinant engineering].' 'What do you want to do?' we'd ask. And we'd get a description of some kind of horror experiment and you'd ask the person whether in fact he'd *thought* about it and you found that he really hadn't thought about it at all. And that's not to call down criticism on anybody because two years earlier I had been in the same position."



Nobel laureate J.D. Watson and Sydney Brenner confer amid the cypress.

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Thus it was, in July of 1974, that the letter first appeared, published simultaneously in the slick pages of three major scientific journals — the first major self-regulation appeal to the scientific community since the early Forties, when physicists agreed to deny German access to nuclear data. The letter, signed by 11 leaders in the field, filled only a single page—headed "Potential Biohazards of Recombinant DNA Molecules"—but that single page said enough to send a major tremor through the entire international fraternity of molecular biologists. In blunt language, the statement called for a global moratorium on certain experiments in the brand-new field of recombinant DNA engineering—specifically those which threatened to introduce antibiotic resistance, oncogenicity or the other poisonous qualities known generally as "pathogenicity" into microorganisms that presently do not possess these abilities.

But wait a minute. One would think we already have all of the dangerous microbes we need and bacteria seem to be learning antibiotic resistance quickly enough on their own. So who the hell would *want* to do these experiments in the first place?

Lots of people, it develops—and for some fairly good technical reasons. Antibiotic resistance, for example, just happens to be a very convenient genetic trait to transplant. Once the previously nonresistant bacteria have been modified through recombinant engineering, one can find out whether the genetic transplant has taken simply by dosing the modified bugs with antibiotic. If the bacteria die, the experiment is a failure. If they live, the experiment is a success and one likely has learned something fairly valuable about molecular biology. And at the same time created a brand-new strain of antibiotic-resistant bacteria. And equally, how will one ever figure out how cancer works without using the same techniques to take a cancer virus apart?

So reaction to the letter was both swift and vocal —from the decision of the Medical Research Council in Great Britain to make the suspect experiments virtually illegal to the opinion expressed by one microbiologist at an international conference in Switzerland: "You should not hamper basic science. You cannot slow down research."

"Such experiments," the letter warned, "should not be undertaken lightly." And that was in fact part of the problem: Nobody in the field was taking them *lightly*. Molecular biology had been in the experimental horse latitudes too long and, as another attendee at the Swiss conference observed: "This new approach is likely to revolutionize not only our knowledge of gene and chromosome organization but possibly of genetic diseases, perhaps cancer. The potential benefits are so great that this sort of research is gaining uncontrollable momentum. . . ."

Potential benefits. In a crasser perspective this seemed, as well, to be one of those periods of scientific inquiry when the prizes and the plums hang from a somewhat lower bough on the tree of knowledge. One of the signatories of the letter—Nobel laureate James Watson, who, with Francis Crick, first deciphered the structure of DNA two decades ago—himself describes that peculiar brand of breathless scientific competition in his book *The Double Helix*.

So feelings were high and—as some of the signers of the letter were themselves pioneers in the field—there were even dark mutterings about the moratorium as "intellectual lockout." But even so the moratorium was almost universally observed during the eight months between the publication of the letter and the first sunny Sunday at Asilomar. And by that time there was no desire to talk about the few violators. Instead the questions were of the immediate future: Under what conditions may we proceed with these experiments?

And far more urgently: When can we start?

First Session

Monday morning, the full moon still bright over the blue-black Pacific, the breakfast bell tolls in the center of the compound and soon the molecular biologists begin to file through the dawn light and into the redwood chapel that will serve as center for the next four days.

Inside, the chapel is dim and gloomy, with theater-type seats, exposed beams and an elevated stage that, even stripped of ecclesiastical accoutrements, is still unmistakably reminiscent of an altar. Debating the ethics of human interference with the mechanics of evolution in a church at the edge of the immense saline test tube where it all started: Rarely does one find one's metaphors so cheap—or so apt. "Here we are," a young scientist from the East Coast will tell me later that night over beers, "sitting in a chapel, next to the ocean, huddled around a forbidden tree, trying to create some new Commandments—and there's no goddamn Moses in sight."

The caliber of the conference is such that, should some wrathful hand wipe out this chapel and the scientists within, it would likely set back the progress of molecular biology a decade or so. And to add cheap irony to cheap metaphor—it is immediately clear, this morning, that of this vanguard now fiddling with the most basic mechanics of reproduction, no more than six are female.

And no real candidates for Moses, either, among the jet-lagged congregation. Paul Berg, the Stanford biologist who headed the moratorium group, just doesn't look enough like Charlton Heston. This morning he appears the quintessential young California academic: tanned, intense, athletic, in studiedly casual sport clothes and a suitably collegiate sweater donned against the early morning Monterey chill. He might as easily be dressed for sailing or an early round of golf, but here he is, standing onstage in front of 140 international colleagues, expressing once again a concern that some privately consider obsessive: "What is new," he says with flat certainty, "is that recombinant DNA can now be made from organisms not usually joined by mating—and hence can give rise to DNA molecules not previously seen in nature."

"If we come out of here split and unhappy," says another conference organizer—a young, successful molecular biologist named David Baltimore, clad in trim beard and elaborately embroidered Levi jacket —"then we will have failed the mission before us."

The first session rolls on well past the lunch bell, much of it fetchingly anal. A major question, vociferously argued, is just how likely it is that these *E. coli* K12 bacteria, so long laboratory pampered, will survive in the human gut, should they escape their test tubes. A series of British researchers demonstrate a consistent penchant for mixing K12 cultures into half pints of milk, swallowing same and then monitoring their subsequent stool for evidence of bacterial survival. The topic offers some opportunity for drollery ("A nice, quiet, boring person," someone describes a chart of stool flora, "as far as his colon is concerned"), but by the end of the session, the implications of K12 ingestion seem far from resolved.

But by the end of the same session, another implication seems all too clearly defined: pure and unadulterated paranoia.

The Press, the Public and Paranoia

"These proceedings," announces David Baltimore at the opening of the first session, "will be taped—for the archives and for review, not for release. And anyone who does not want to be taped may ask and the machine will be turned off."

Immediately someone rises in the audience. "But what about the *press*?"

There is a brief silence in the still somnolent audience. What *about* the press, with those nasty Sony cassette machines perched stage left, right beside the official Academy of Science sound equipment?

After some deft reassurance by the NAS press officer, a vote is taken. The press is permitted, with many abstentions, its recording equipment. But it is not, by any means, yet permitted any real welcome.

And that's no surprise to the press. By now the vibes are unmistakable—and have been so since first application for permission to attend Asilomar. Press attendance was not actively encouraged by anyone involved and in the case, say, of a reporter from Rolling Stone, it took some persistence even to find out whom to *ask*. A writer from Washington told the conference organizers straight out: "A secret international meeting of molecular biologists to discuss biohazards? If the press isn't allowed, I'll guarantee you nightmare stories." Or as a journalist from Southern California said: "The scientists loved the press when we got Nixon. But when we start hanging around their own back yard, they get very nervous."

...gle of molecular biologists, on chapel steps.

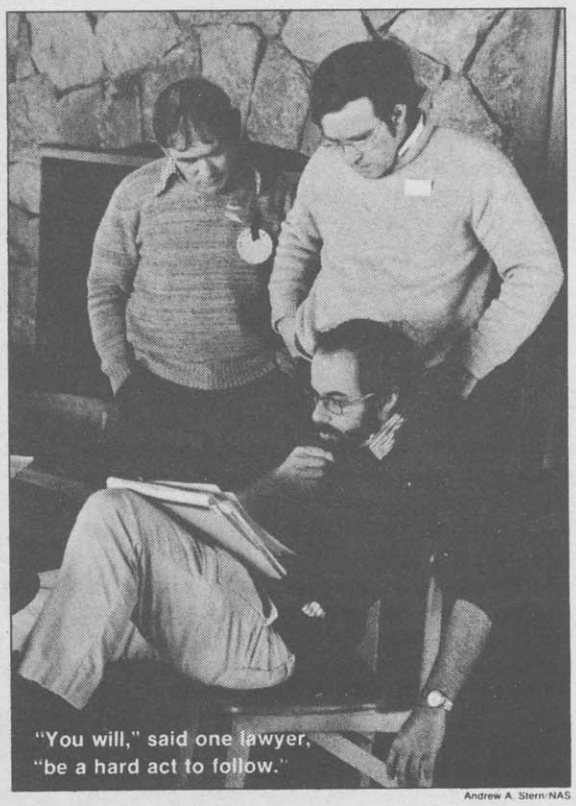
Andrew A. Stern NAS

Nervous indeed. One young researcher from Stanford—a fellow sufficiently in the vanguard to have had a variety of plasmid named after him—is so compulsively press shy that even when the official photographer approaches him at the chapel entrance, he retreats, face covered, like a newly busted big-time mobster hiding behind his fedora on the steps of a precinct house.

It seemed almost a paradigm of the unsatisfactory relationship between the press and science. Paranoid behavior is guaranteed to engender the journalistic suspicion that something is up. And the more attention the press paid, the more paranoid the attendees became—and not entirely without reason. A suitably hysteric story about the antics of an international cabal of biologists devoted to some blackly humorous campaign of creating new cancer viruses might be just the thing to stampede Joe Public.

And the press was not always altogether reassuring; after four days of intense sessions, some individuals were still asking questions that suggested they had passed the previous days locked in a very dark closet. As some cornered scientist explained for the fifth time a fairly fundamental concept of cell biology, the question in his eyes was clear: How the *hell* does this befuddled individual with the notebook think he's going to explain the subtleties of plasmid engineering?

Or perhaps even worse were the questions clearly designed to elicit the quotable lead for some mythic housewife to digest over morning coffee: "Dr. X, would you say that this technique of plasmid engineering is the most important advance in science since the invention of the mammal?" Or: "Dr. Y [who has already expressed the utter impossibility of answering this question at least half a dozen times], in how many years will we have a genetic cure for diabetes?"



"You will," said one lawyer, "be a hard act to follow."

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Welcome or not, however, the press was there, hunkered down in the front row, Sonys turning, and there was really nothing to be done about it. By the end of the sessions, it was clear that press presence caused the conference attendees both some discomfort and some extra efforts toward public caution.

And that, finally, seemed fairly healthy.

Happy Talk

"This is what we know how to do," one Eastern microbiologist notes plaintively midway in the proceedings. "This is what we're used to doing. I mean, we all get together, we want to know what everybody else is doing."

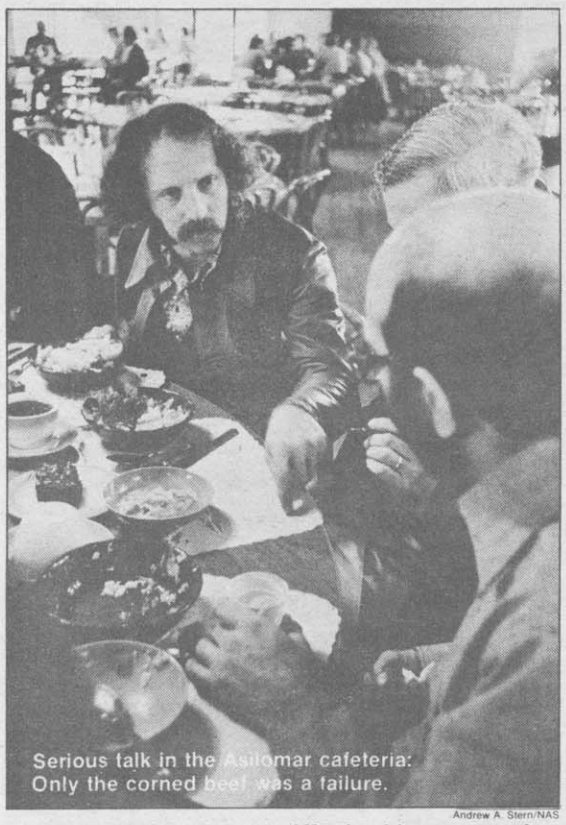
Indeed. During the first two days of sessions, it becomes immediately clear that the conference attendees would really rather talk about almost anything than the issue at hand. "Molecular biology of bacterial conjugation and conjugative mobilization of plasmid and other DNAs," say, or "molecular cloning of DNA as a tool for the study of plasmid and eukaryotic biology," each illustrated with slides that appear either like children's plastic building blocks or the tracings of snails in debris-scattered rain puddles.

The talk is exceedingly technical and wanders over a spectrum of topics—some including information sufficiently original that afterward researchers queue up at Asilomar's two pay telephones to relay the word back to their laboratories.

It all goes very smoothly—this is, after all, what these people know how to do—and the presentations offer an interesting inside view of the potentials that the popular press has so long trumpeted for genetic engineering.

At one point, for example, a tan young Southern Californian clambers onstage holding a three-foot-tall weed, freshly harvested from a Monterey roadside, as a colleague passes out similar plants to each row of molecular biologists. It is a legume, says the plant specialist, and if one shakes the dirt off, it's possible to see the tiny nodules on the root structure that "fix" nitrogen—adapt it to forms useful to living organisms—directly from the soil. Not a bad trick, since most world food crops are not legumes and thus require doses of artificial nitrogen fertilizer—created, in turn, from a commodity somewhat scarcer than dirt: petroleum.

Clearly, if one were able to isolate the gene that teaches nitrogen fixation and then ally that, say, with a *wheat* plant—then one might just have one hell of a food crop. One in five human beings already harbors a strain of nitrogen-fixing bacteria in their gut; the same bacterium is almost universal among certain New Guinea tribesmen who eat ten pounds of sweet potatoes a day. It might not, the plant special-



Serious talk in the Asilomar cafeteria: Only the corned beef was a failure.

Andrew A. Stern/NAS

ist suggests, be such a difficult thing to teach a plant. . . .

It is obviously a far more imminent prospect for genetic engineering than dial-a-baby. So also is the possibility of recruiting some remarkably cheap labor in the pharmaceutical industry. One might, say, isolate the gene that codes for insulin production, pump that gene into a colony of *E. coli* and then sit back as the colony, suitably well fed, begins to pump out pure insulin. The prospect is sufficiently realistic that the conference includes representatives from the research arms of drug manufacturers Merck, Roche, G. D. Searle—and even General Electric.

A Primitive Tribe of Beach-Dwelling Molecular Biologists

But the state of the art, entrancing as it is, isn't really the issue at hand. Yet each time the real issue arises—as, say, when some advisory group, previously appointed, introduces "Proposed Guidelines for Plasmid-Cell DNA Recombinant Experiments" —the proceedings rapidly develop the appearance of some obscure primitive tribe eons ago, accidentally stumbling by trial and error onto the secret of parliamentary procedure.

Odd, one might think, that a roomful of the leading minds on the leading edge of science can't agree on how to run a meeting. But there is little evidence of any concerted drive toward organization here. Sometimes the derailments are benign: An irrepressible gentleman from Switzerland monopolizes a microphone for a baffling ten-minute dissertation on scientific ethics, by the end of which it is difficult to decide whether the researcher's English or his thought processes are the more twisted. Or some well-intentioned American drones for an equivalent period about his role in the licensing of an obscure vaccine some years earlier, which, it grows quickly clear, has very little to do with anything. Or the entire discussion lurches off into a swamp of technical detail: "Well, why can I use *Xenopus* DNA under low risk conditions when Josh Lederberg has to use *Bacillus subtilis* under moderate risk?"

But sometimes it's not clear precisely *what* is at stake. One afternoon a paunchy and influential Englishman, who each morning in the Asilomar dining hall salts his cornflakes, rises to quote a sentence from one of the working papers.

" 'For our purposes,' " he recites, " 'pathogenicity and virulence are defined similarly as "the capacity to cause disease." ' " He pauses briefly and then announces in precisely cultured intonation: "This must rank as the greatest oversimplification of all time."

The panel of seven who drafted the report, arrayed behind microphones onstage, looked slightly hurt. Their report is, after all, 35 single-spaced pages, and getting scientists to write 35 single-spaced pages of anything is no small accomplishment. The Englishman, however, proceeds then to sharply question the qualifications of the whole bunch of them.

Finally the panel leader cuts him off, thanks him for the "input" and asks for a written critique. "This is, after all," he apologizes, "a rather terse document."

The Englishman continues to stand. "You could have fooled me," he observes acidly.

Alterations will be made, the panel leader assures him; after all, this working document was assembled in only six days.

"And why couldn't you do it in six days?" the Englishman wants to know. "After all, the Lord created the world in only seven."

The Russians

"These Russians," an elderly microbiologist from Wisconsin says one night at dinner, "they just send over the old guys from the academy [the politically powerful Academy of Sciences of the U.S.S.R.] who don't know *anything*. You ask them something and they hedge around—and it's not that they're hiding things . . . they just don't *know* in the first place."

The Russian presence is in fact somewhat puzzling. The Soviets number five: two oldsters, in black suits and narrow ties, both with thick, healthy shocks of nearly pure white hair, along with two younger scientists—"The Rolling Stones? Iss a jass band, no?" —and a charming, dapper, San Francisco vice-consul, performing chaperon service.

The oldest is 88 and the talk at Asilomar has him the highest of honchos in Soviet biology. Talk has it also that, due to the massive doctrinal detour posed under Stalin by Trofim Lysenko's curious evolutionary notions, Russian molecular biology is not yet precisely state of the art. And, in fact, the eldest Russian's primary contribution to the conference seems to be his stolid, front-row use of a small pocket camera to photograph the charts and slides projected onstage. His diligence provides more than a bit of amusement, however: For unfathomable reasons, he persists in using a bright miniature flashgun each time he photographs the screen and the consensus is that he may have taken home a bit less than expected.

The oldest Russian's English seems baffling as well; our few conversations stall quickly, as I admit in my college Russian that "I do not speak very much Russian," to which the aged academician smiles, nods and pronounces somewhat ambiguously: "Berry goodt!" What, I wonder, does he expect to get out of these presentations, all in the most technical of English? Until one day I hear the oldster speaking to a science reporter from the East, an attractive young brunette who has fetchingly left the top two buttons of her thin cotton blouse undone. For her the old Russian's English flows like the Volga.

At the final session on Wednesday night, there is a handout at the door: a xerox of a telegram, transmitted through an intermediary in Toronto and signed by a young Russian named Alexander Goldfarb. Goldfarb has a fairly thorny request for the conference:

. . . TO DISCUSS AND EXPRESS YOUR OPINION ON THE POSSIBILITY OF USING A RESEARCH ON ENZYME RNA POLYMERASE FROM ESCHERICHIA COLI PARTICULARLY BY ITS MODIFICATION INDUCED BY P-EVEN BACTERIOPHAGES FOR WARFARE.

HOWEVER CRAZY THIS REQUEST MAY SEEM TO YOU, THE FACT IS THAT LAST SPRING MY APPLICATION FOR A VISA TO EMIGRATE TO ISRAEL WAS TURNED DOWN BY THE SOVIET AUTHORITIES JUST BECAUSE THIS RESEARCH WHICH I WAS DOING IN THE BIOLOGY DEPARTMENT OF THE KURCHATOV INSTITUTE OF ATOMIC ENERGY, MOSCOW, WAS "CONSIDERED IMPORTANT FOR THE STATE SECURITY OF THE U.S.S.R."

Goldfarb's request is something of a tall order. Plasmid engineering, in suitably amoral hands, might produce microbes to make superanthrax or concentrated botulinus toxin look like German measles. There seems enough hazard already in pure and simple carelessness, and at the outset of the conference it has been agreed that the issue of new horizons in biologic warfare will not even be raised; for the moment, it is first things first.

And hence Goldfarb's request requires no action and in fact elicits little comment. Except for a reporter who, after the evening session, follows the two elderly Russians out into the cool night air.

Immediately one of the younger Soviets slides in to cover the situation. "Of course," he says in flawless English. "We knew this might come; we had been briefed."

What will happen to Goldfarb's appeal?

The young Russian shakes his head. It is standard, he explains, that anyone associated with security work is required to wait three to five years, after leaving his job, before leaving the country. It is as simple as that, he says, and there is nothing that can be done.

So the Soviet Union considers molecular biology as militarily significant?

It is as simple as that, the Russian repeats, and there is nothing than can be done.

At this point the older academician, who has been observing this exchange with glacier-blue eyes, suddenly shakes his head. "We knew," he says shortly, "we knew he was writing these letters. He has been writing these letters to everyone. He started out writing these letters to the heads of state and now he is writing them to the porters at the door." He snorts, shakes his head again and then the three Russians move into the Monterey night.

"Jesus," says a young American scientist, hair touching his shoulders, who has listened to the last portion of our discussion. "Goldfarb's fucked," he says. "I bet his next assignment is cryobiology."

Cryobiology?

"You know," he nods. "In Siberia."

Disarming the Bug

"What I would like to do," says Sydney Brenner late one afternoon, "and what certainly seems incumbent upon me, is to erect the highest barriers possible between my laboratory, where the work is performed, and the people outside."

Brenner, a compact Englishman in his 40s, with bushy eyebrows, gleaming eyes and nonstop animation that blend to an impression midway between leprechaun and gnome, soon emerges as the single most forceful presence at Asilomar. Repeatedly, when the sessions wander off into a technical morass that threatens to engulf larger considerations, Brenner rises to redirect deftly.

"Does anyone in the audience believe," he asks, in one such redirection, "that this work—prokaryotes at least—can be done with absolutely no hazard?" There is no immediate response. "This is not a conference," Brenner goes on, "to decide what's to be done in America next week. If anyone thinks so, then this conference has not served its purpose.

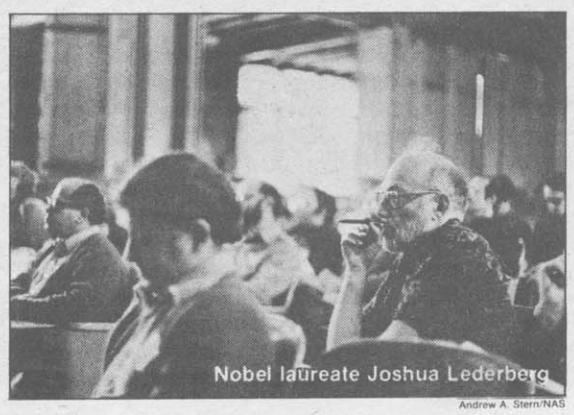
"In some countries," he says, "this would be done by the government, and once guidelines were set and you broke them there would be no question of peer censure—the police would simply come out and arrest you."

This is an opportunity, Brenner concludes, for scientists to show that they can regulate themselves —"to reject the attitude that we'll go along and pretend there's a biohazard and hope we can arrive at a compromise that won't affect my own small area, and I can get my tenure and grants and be appointed to the National Academy and all the other things that scientists seem to be interested in."

Brenner—a leader in the field—also takes charge of a series of afternoon sessions devoted to a task called "disarming the bug." The sessions are lively and well attended and they represent a curious tangent of mankind's new involvement in the processes of evolution. These people are trying to create novel organisms that are by design incapable of living in the real world.

"Self-destructing vectors" is one phrase for the new bugs. A "vector," in biologic terms, is a mode of transmission; "ecologically disabled organisms" is another. What these will be, ultimately, are bacteria or bacterial viruses—tools in plasmid engineering—that will be unable to live outside the laboratory. Should they manage an escape, even into sewer or stomach, they—and their novel genetic content—will die without reproducing.

Brenner has great faith in the notion of self-destructing vectors; such faith, in fact, that the first of the proposed strains, dubbed "Mark One," has been



Nobel laureate Joshua Lederberg

Andrew A. Stern/NAS


Conference organizer Paul Berg

Andrew A. Stern/NAS

renamed by cynics "Mach One"—in honor of the speed with which Brenner believes it can be produced.

Even so, Brenner has his doubts about the course that the biohazard question will run in the United States. He is, after all, from a country that has already had an exceedingly expensive biohazard accident—and one, moreover, where laboratory technicians are sufficiently organized that they can shut down a laboratory when a biohazard question remains unsolved.

"The competitive nature of the institutions themselves can affect the situation," he says one afternoon on the chapel steps. "Sooner or later, at some place like MIT or Stanford, some laboratory assistant may well contract something like leukemia—and he will sue the place for everything they've got."

At the time, it seems a fairly pessimistic scenario—but by the time Asilomar lurches to its conclusion, it grows clear that Brenner has described an issue that ultimately proves thoroughly telling.

Chosen Sons of Alfred Nobel

"Nobel laureates can't believe in their own scientific fallibility," says a young molecular biologist one day at lunch. "I've seen lots of them and it's common to the phenotype."

"If you're a Nobel laureate in this country," agrees a plant biologist, "then there's nobody who can touch you."

Perhaps so. While William Shockley might disagree, it's clear that the two American Nobel laureates at Asilomar—Joshua Lederberg from the West and James Watson from the East—exert powerful presences during the conference proceedings. And not always in a terribly popular fashion.

Watson and Lederberg seem almost perfect opposites. Lederberg is a large, bearded, well-nourished man, given to wearing loose sport shirts, brightly patterned in Hawaiian style. He has the healthy look of the senior California academic who spends weekends in hot baths at Esalen or working in a manicured garden. Watson, on the other hand, seems almost to cultivate the persona of absent-minded professor: tall, pale, thin, shirt collar turned up, wispy brown hair tugged so constantly that it stands out from his head in total disarray. He speaks with a regular punctuation of grimaces and, in the midst of any given sentence, his gaze can wander off into space; a consummate 2000-yard stare.

"If we can't communicate the tentativeness of this document," Lederberg says early one afternoon in the chapel, "then we are in trouble." There is, he suggests ominously, "a graver likelihood of this paper crystallizing into legislation than some of us would like to think."

At this point, one major approach to the problem has been to classify experiments in six numbered categories of risk—from those sufficiently safe that they can be done with only standard precautions, through class-IV, which require a fairly complex and costly set of containment procedures, to class-VI, which at this time, goes the recommendation, simply should not be attempted. Lederberg fears that such detailed restrictions might be taken too literally—and inflexibly—by some well-intentioned legislative body and thus thoroughly garrote future research. An alternative suggestion has been to create three less specific risk categories: high, moderate and low.

But shouldn't, someone asks, we benefit from all the experience we already have?

Watson, slumped low in the middle of the audience, mutters to his neighbor: "But there *is* no experience."

"I have to emphasize," says the onstage panel leader, "that there was a great deal of consensus among the members of our panel."

"So is there in the State Department!" Watson exclaims quietly. He sits for a moment, then whispers to his seat mate: "These people have made up guidelines that don't apply to their own experiments."

"Stand up and say it," his companion urges softly. "You can say it; I can't."

Finally, prompted, Watson rises to ask the question: Why, according to the panel, is this particular form of DNA considered safer than another?

The chairman frowns. "It wouldn't be fair for me to answer that question," he says and turns to the panel. "Anybody like to defend *Xenopus*?"

Nobody really wants to and finally Watson sits, shaking his head. "He refused to answer the question," Watson announces softly to anyone within range.

Paul Berg stands to get the session back on course. "We have to make a decision," he says. "Can we measure the risks numerically?"

Watson, sotto voce, explodes: "We can't even *measure* the fucking risks!"

From here on, the discussion begins to fragment. A long-haired researcher from Alabama suggests, aptly, that "anything that comes out of this meeting should self-destruct in 12 months." Someone from Stanford wonders what will happen when local committees have to assess biohazards: "If we can't agree on the danger of experiments here, imagine the situation of a local university committee!"

"Legislation," says one experimenter, "is inevitable. I can't believe that we'll be allowed to continue to control ourselves. But something that could set back the progress of science even more than legislation is if, in a few years, there's a sudden epidemic around Stanford, say, or Cold Spring Harbor."

Finally, just before the dinner bell rings, an English researcher rises to suggest that the problem here is sufficiently complex that those in attendance should go home, brood a bit and then offer suggestions in writing.

"So you don't believe we can arrive at a statement by Thursday noon?" Berg asks him.

The Englishman pauses, shakes his head. "I don't know," he says finally. "I don't know."

"But we are the people," says a young American, "who are supposed to *know* about this and we can't go home from here and decide nothing."

"But we haven't," says Lederberg, "been told what the vector will be. Unless Berg and the organizers tell us the utilization of this document, I'm going to be very hesitant about making any recommendations."

Berg rises again. "If our recommendations," he says, "look self-serving, we will run the risk of having standards imposed. We must start high and work down. We can't say that 150 scientists spent four days at Asilomar and all of them agreed that there was a hazard—and they still couldn't come up with a single suggestion. That's telling the government to do it for us."

At this, Watson, inspired, is up like a shot: "We can tell them they couldn't do it either!"

A Bit of Little-Known Recent History

Tuesday afternoon at Asilomar the early spring air is crisp and the sky a cloudless Kodachrome blue. Inside the chapel, however, the curtains are drawn, the air is still and heavy and only an occasional shaft of sunlight manages to penetrate, striking a balding head here, a graying one there. The texture and color in the rustic chapel this afternoon are early Rembrandt; the content of the program is pure and simple Modern Dilemma.

The final speaker this afternoon—Andrew Lewis of the National Institutes of Health—has the distinction of being the only member of a working group who felt it necessary to submit a minority opinion. ". . . Given the limited amount of information available at this time," he wrote in that dissension, "I believe that the risks associated with the widespread, semicontained use of this procedure exceed the rewards from the information to be obtained."

Lewis—in his 30s, conservatively dressed, unmistakably serious—also offers a singular perspective on the problem. He is the first person in this country to be burdened with the distribution of a brand-new, laboratory-created—and potentially hazardous—variety of cancer virus.

Adenovirus 2 is a member of a common family of viruses found, usually fairly harmlessly, in human beings. Simian Virus 40 is a virus found in the kidneys of certain Asiatic monkeys. SV40, however, has also been shown to cause tumors in newborn laboratory animals and, moreover, to cause similar cancerous changes in human tissue in test tubes. In 1969, the isolation of an accidental hybrid between adenovirus 2 and SV40 was reported—apparently combining genetic material from both viruses and, moreover, capable of independent reproduction in both human and monkey cells.

The new hybrid virus represented an altogether unknown hazard to human beings—and also an exceedingly interesting subject for cancer research work. And thus it was that Lewis found himself responsible for distributing a virus strain of unknown pathogenicity to other research laboratories.

It wasn't as if SV40—for a monkey virus—hadn't already had enough to do with human beings. SV40 was not discovered until the early Sixties—and by then a considerable amount of polio vaccine had already been grown in monkey kidney cultures ripe with SV40, which in some cases survived to inhabit the vaccine. Thus, from ten to 30 million Americans presently between 15 and 35 years of age received, along with their brand-new polio vaccine, a dose of live SV40.

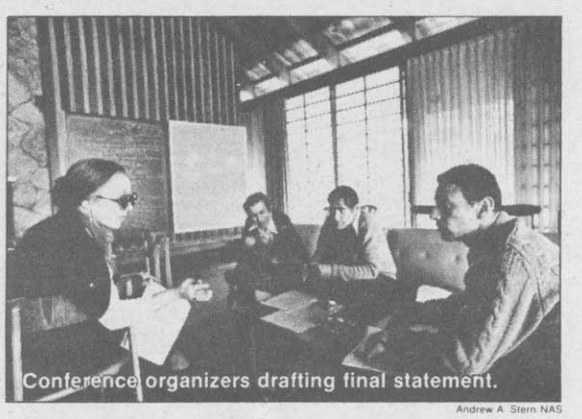
Well. More than a bit of discreet medical surveillance has been directed, by now, at known SV40 recipients—and thus far there has been no evidence of any mass malignant onset, which, considering the numbers involved, could make thalidomide appear small potatoes in the history of self-inflicted human suffering. A handful of recent studies, however, has suggested the presence of SV40 in association with some thoroughly unpleasant human tumors and neurologic disorders. And so the scrutiny continues. If medical science has learned anything about viruses thus far, it is that they are tricky.

Andrew Lewis agreed to distribute seed stocks of the first SV40 hybrids, along with a letter describing "reasonable precautions" and requesting that the recipient laboratory distribute none of the virus on its own. But by then, four more hybrid viruses had been located—all equally suspect—and these Lewis refused to send out.

"The question we faced," Lewis says this afternoon at Asilomar, "was whether one individual had the right to decide to distribute potentially hazardous laboratory-created recombinants." The reaction from the research community was immediate: threats of congressional action or administrative pressure from NIH—even the suggestion of a group letter to *Science*. And, on the other hand, concerned scientists warned that if Lewis went ahead with the distribution, they would file for a federal environmental impact statement.

"I felt," says Lewis, "that voluntary compliance by interested investigators was the most satisfactory method," and so he decided to require a formal document from each laboratory that requested the viruses, stipulating that the researchers assumed full moral and legal responsibility for the viral agents.

Fifteen months later at Asilomar, Lewis is no longer so certain about volun- [*Continued on 74*]


Conference organizers drafting final statement.

Andrew A. Stern/NAS

PANDORA

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tary compliance. "Several major laboratories," he says, "have thus far not supported the Memorandum of Understanding and Agreement. In addition, our original request to restrict the distribution of the first hybrid appears to have been ignored by one or more of these same laboratories."

Lewis's opinion, clearly, is not popular. The audience is cold and midway in his presentation, Lewis begins to lean intently over the podium, grasping his pointer, straight up, like a spear carrier in an Italian opera. The source of the hostility is no mystery: This conference is, after all, *about* self-regulation — and regardless of Lewis's unfortunate experience, one bad apple need not spoil the barrel.

Or does that depend on the apples?

The Lawyers: Reality Therapy

By Wednesday night—with only a single morning session remaining—the situation at Asilomar seems as unsettled as the Monterey weather. The mild blue skies have begun to turn and by now a massive bank of thick gray fog lies a mile or so off the coast, sending in low, damp clouds both morning and evening. The conference meals have started to deteriorate as well and this evening's corned beef and cabbage barely achieves summer camp standards. Worst of all, however, is the possibility that the conference, enmeshed in bickering, may not actually be able to arrive at a group statement. But clearly, with three days of talk about biohazards thoroughly soaked up by the press, it is too late to stop now. The question remaining is exactly what to do about it.

Part of the impetus, as it develops, is about to come.

The Wednesday night program looks fairly innocuous: presentations by lawyers regarding ethics and legal liability. Lawyers, of course, are supposed to have some knack for public speaking, as opposed to—as anyone who has attended a scientific conference can testify—men of science. The evening promises, at least, a nice diversion.

And so, at first, it seems. The first speaker, dapper, pleasant, goateed — the husband, in fact, of the only female conference organizer — spends a mild-mannered quarter-hour eloquently dissecting a dictum familiar to all medical students—first of all, do no harm—and concludes with a fairly abstract three-part analysis of risk versus benefit that covers, in thorough generalities, just about exactly the major issues of the past three days.

So far, so good. Analysis like this isn't going to help anyone decide between numerical hazard rating and high/moderate/low, but it's nice to hear just how important the responsibility *is*. And just how complicated the problem.

The second speaker—a professor of international law—promises to be equally entertaining. He approaches the podium in sports coat and open-collar shirt, appearing not much older than 22. His demeanor, however, is distinctly confident as he starts with a nice joke: A scientist and a lawyer are arguing about which of theirs is the older profession. The argument goes back and forth, from Pericles to Hippocrates to Maimonides to Hammurabi, until it reaches all the way back to God.

God, the scientist states, must have been a scientist, to have brought order out of chaos.

Yes, the lawyer responds. But where do you think the chaos came from?

The joke turns out to be less joke than promise, as the young lawyer proceeds into a merciless "outsider's analysis" that, within minutes, has jaws dropping all over the chapel. Much of the conference, he suggests, has been irrelevant to the central issue.

The audience is suddenly very quiet.

Many of the specific arguments, he goes on, have been equally inapplicable. "Academic freedom," he points out, "does not include the freedom to do physical harm." And "prior restraint"—a notion advanced the previous day by a Nobel laureate—makes perfect sense when it involves restraint from doing physical damage.

"This group," the young lawyer suggests flatly, "is not competent to assign overall risk."

What? But that's the *point* —most here, likely, would consider themselves *uniquely* competent. Who else could do it?

"It is the right of the public," continues the speaker, "to act through the legislature and to make erroneous decisions."

Jesus. Now that's a hell of a reassuring thing to hear from a lawyer and it's clear, in the still air of the redwood chapel, that the audience is growing just a bit discomfited.

And it's only worse when the lawyer suggests a hypothetical situation wherein Congress might insert its grubby political fingers into the delicate process; "Congress" manages to draw a low but audible groan. Legislation, however, might not be all bad, he explains: The law might provide, say, for liability in cases of biohazard accidents.

But that, by now, seems faint comfort. "Legal institutions," the young lawyer intones in civics-class fashion, "are a part of your world,

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whether you like it or not." And with what the conference attendees are into, he concludes, it's time to involve those institutions.

Well. There is a low buzz of conversation as the next speaker is introduced; all of this really isn't that pleasant, compared to the technical papers. Clearly, one group of slightly arrogant professionals are here being dressed down by another group of at least equally arrogant professionals. And the lawyers probably make more money, too.

But the best is yet to come. The final speaker is short, middle-aged, fairly nondescript in mismatched suit and tie and thick glasses. One would have noticed him earlier only because of his ceaseless squirming during the technical sessions—the scientists did not squirm; they either paid attention and took notes or went to sleep. This speaker appears something of a manic milquetoast but by the time he is behind the podium and has completed a sentence or so, his dry sharp delivery makes it clear that this is the lawyer who slices one mercilessly to very tiny ribbons in the witness box.

Which is, coincidentally, precisely his topic: "Conventional aspects of the law," as he puts it, "and how they may sneak up on you—in the form, say, of a multimillion-dollar lawsuit."

Hmmmm. Now, abruptly, the audience is *very* quiet. The subject of legal responsibility has really not yet been dealt with in the nitty-gritty terms of "Who, exactly, gets sued when something goes dreadfully wrong?"

This lawyer aims to explain and, having himself just squirmed through three days of abstruse technical jargon, he takes some relish in trotting out his own — torts, liability, proximate cause, OSHA—and illustrating just how finely—if not fairly—the wheels of law can grind.

Professional negligence, the lawyer suggests, is a failing that finds juries exceedingly unsympathetic. Take the case of the ophthalmologist in Oregon who lost a malpractice suit on his failure to perform a glaucoma test on a young and asymptomatic patient in whom the chances in glaucoma were one in 25,000. Judges, he points out, are experts only in law—and juries, quite intentionally, are experts in nothing at all.

By now, the gathered molecular biologists are conspicuously attentive.

Oh, it's not totally hopeless, the lawyer reassures. If, say, a burglar were to break into one's lab, steal a vial of deadly virus and then strew the contents all over Brooklyn, then maybe—just maybe—the intervention of a third party might get one off the hook. Or if one's work is for national security purposes, then one is probably also fairly immune from prosecution.

But, of course, there are already laws under which recombinant engineering might be controlled: OSHA, for example—the Occupational Safety and Health Act—could conceivably be invoked to protect laboratory workers. According to OSHA, the lawyer explains, "the work place must be free of hazard. Not relatively free," he says. "The statute says *free*." And the person who sets those standards is — the Secretary of Labor.

Jesus God. All of this, clearly, is the most violent intrusion of the real world into these proceedings thus far. Some goon from the Department of Labor, waltzing into one's lab for a surprise inspection, on the outcome of which might hang a $10K fine. Or the notion of one's own laboratory technician, bizarrely diseased and setting out for revenge on the basis of a bloodless legal principle called "deepest pockets." While there has been no lack of real and humane concern among the attendees these past three days, there has been something about this brief legal seminar that has brought home, rather forcefully, just how *unpleasant* things could get.

Within minutes, however, the molecular biologists have rallied to the defense, the more vocal bravely citing legal precedents—fetal experimentation, medical research on prisoners—as argumentatively as possible. It is, however, as effective as if one of the lawyers had earlier risen to question a certain enzymatic manipulation of a lambda bacteriophage.

Finally, Nobel laureate Lederberg stands and, with some eloquence, presents an intricate analogy involving the risks and responsibilities of accidentally bringing home a deadly African virus.

"That argument," says one of the lawyers, "with all due respect, is almost entirely beside the point. If we are remiss about our international travel regulations, we should move to correct that situation, rather than taking it as reason for being equally remiss about our approach to the biohazard question."

Lederberg returns to his seat, big tan arms folded across his chest like a wounded Buddha. The next question is more along the lines of, *precisely*, who is likely to get sued? And by the end of the evening, one of the lawyers is actually advising the conference to look into the possibilities of extended personal liability insurance. "At least," he says, "then you won't have *quite* so much to worry about."

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FINAL SESSION

Thursday morning provides the grayest sky thus far at Asilomar. "At noon," Paul Berg announces at 9:00 a.m. inside the dim chapel, "I would like to terminate this meeting and I hope that by noon we can reach a point where such termination is possible."

Berg and his organizing committee have done their best toward that goal: up all night revising, condensing, rewriting the working papers and discussion of the past three days into what is now a freshly xeroxed five-page handout titled "Provisional Statement of the Conference Proceedings."

The statement, clearly, is a compromise: The six-category classification of risk has now, uniformly, been condensed to low/moderate/high. And there is no flat proscription of the experiments that some have earlier called unreasonably hazardous.

But it is still, in context, a strong document: If adopted, many researchers will have to go home and spend thousands of dollars on laboratory containment — no small sacrifice in these days of tight funding —to do the experiments they could have done for nothing eight months earlier.

Behind the scientists are the pressure of the lawyers' dark predictions and the hovering presence of the press; before them are the plain realities of research funding. Who, after all, really wants to drop $40,000 on a negative-pressure laboratory equipped with laminar-flow hoods unless it's absolutely necessary?

And so the discussion begins, lurching along, sidetracking, backtracking, and before long, the sense of it is so tangled that weeks later it survives best as a collection of disparate and anonymous exchanges.

"But the input of 150 people has been ignored!"

"If we wanted to ignore the input of this group, we'd all be asleep right now."

"But are you talking about a vote? How will a consensus be arrived at?"

"No. No votes will be taken. We will arrive at consensus through discussion."

"But we *have* to have some kind of vote. Maybe we could ask the press to go away."

"I would like to see something added to this paragraph to say explicitly that there are experiments we can imagine that are too dangerous to perform at present."

"May I respond to that? Based on the split at this meeting as to whether that is a philosophical or a practical question, we decided to put such experiments into the high-risk category. That is by no means a license, since those facilities are both extremely cumbersome and not widely available."

"We have no power but moral censure if someone goes off to Uganda tomorrow and puts General Amin into plasmids. And I don't want to carry the can for *any* of you. I don't want a situation where people can say, well, I did it because the organizing committee said I could. In the end, it is your individual judgment. Certain experiments should have to cross higher barriers of judgment — and others should cross even higher."

"It will save me a great deal of trouble later to get your judgment on a specific case: Would it require a moderate-risk facility, comparable to that used for oncoviruses, to do the following experiment: the transmittal of pSC101 into *Bacillus subtilis*?"

"I'd have to say that it would."

(*silence*)

"I think we're not going to try out all the scenarios here. I think we'll have to move on."

"We modified your decision by drawing a line at cold-blooded versus warmblooded, rather than mammal versus nonmammal, because the avian viruses are known to grow in and transform human cells."

"It's also fair to point out that there are tumor viruses in frogs."

"Might I ask your committee how they propose to deal with the question of type-VI experiments? It has been put to me by people in the U.K. that they can see no possible current experiment involving, say, smallpox DNA. It's not that they couldn't *design* such experiments—it's just that the combination of benefits and risks, at the moment, put these experiments into class-VI."

"I thought we'd agreed to indicate a split of opinion as to whether certain experiments should be ruled not permissible. At this time."

"Could we perhaps, for my benefit as much as anyone else's, test the feeling? Perhaps there *isn't* a split."

"Okay, let me see if I can put the question simply. One view says that there are experiments that should be performed only in the highest containment facilities available today. The other view is that there is a class of experiments that should not be done at all, with present containment methods."

(*a show of hands*)

"Well, it's clear what the sentiment is. The predominant view supports the latter. If we have time, perhaps we can come back to this section.

"Please make your comments brief."

"Is low risk in quotations one thing and low risk without quotations another?"

"I must say, personally, that I really feel, having worked on the plasmid document, that it's been prostituted. And that's all I have to say."

"This refers to someone who goes into a shotgun experiment with the warmblooded beasts and recombines with a safe vector; they may then be reassigned to low risk."

"I think we should remove the phrase 'pharmacologically active agents' and just talk about 'toxic substances.' Insulin could be considered a pharmacologically active agent and some agency might take that very seriously."

"By putting these experiments into high risk, requiring a facility like Fort Detrick—which is probably filled up with some total waste of time —we seem to be discouraging them entirely."

"We're coming up on twelve o'clock."

"It seems to me that there are invertebrates—take mosquitoes, for example — that contain diseases that are dangerous to human beings and if people go willy-nilly joining mosquito DNA with *E. coli*, I'd hate to think I'd get malaria from walking around on the street."

(*front row, sotto voce*): "Huh?"

"How could you get malaria . . .?"

"How could you . . ."

"You're right, taking field-caught mosquitoes and extracting DNA and trying to clone it . . ."

"I just ask to consider this . . ."

(*front row, sotto voce*): "Can they explain . . .?"

"*Say* it."

(*loudly*): "CAN YOU EXPLAIN, please, how a protozoan parasite could result from an *E. coli* and thus cause malaria?"

"We will, ah, take the comment under advisement."

(*front row, sotto voce*): "It's bloody nonsense."

"It's clear that the sentiment is overwhelmingly in favor."

"I don't think that's clear at all."

"Well, as far as I could tell, that would be overwhelming. I think we'll have to go on to item . . ."

"*May I have ten seconds*?"

"Ten seconds."

"Under the pressure of time, very complex issues are being railroaded through. If you're willing to say, in your preliminary document, that that characterizes the nature of the consensus here, then I could go along."

"Okay. We'll move on, then, to the next section."

"Could you ask how many people abstained at including a high-risk rating for insulin?"

"How many people did not

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vote?"

(*show of hands*)

"A small number."

"Let's have the show of hands again. Please! There's no point in abstaining. What are your sentiments?"

(*low mumbling*)

"What are we voting on now?"

Suddenly Sydney Brenner interrupts: "Please," he says slowly, sounding like a sleep-deprived leprechaun. "Could I ask whether, in paragraph six, if the phrase 'this document represents our best assessment of the potential biohazards,' we might change that word 'best' to 'first'?"

For the first time in two hours there is laughter. And then the noon bell tolls for the first time and, shortly, the final vote is taken. The working document, murkily amended, is adopted, with only a few dissenters.

The noon bell tolls again, and as the scientists stir for the early afternoon dash to Monterey airport, one of the lawyers briefly takes the podium. "In many ways," he says, "it was a moving experience for anyone outside the scientific community to watch this group grapple with a very difficult problem. It's been nice being here," he says; "you will be a hard act to follow."

But the act, of course, has only just begun.

Conclusion: Human Sex as Moderate-Risk Experiment

"There's only one way to control scientists in institutions," a young researcher noted midway at Asilomar: "Take away their money."

Less than 24 hours after the tentative consensus at Asilomar, a select group of scientists and administrators sit at a polished wooden conference table in an ornate San Francisco hotel meeting room. They represent the National Institutes of Health and their job, this bright morning, is to transform the general conclusions of Asilomar into formal guidelines that involve funding restrictions, local biohazard committees, the variegated details of specific enforcement.

This is, of course, what many conference attendees feared most. "Already," a microbiologist admitted one night by the dormitory fireplace, "we spend two months a year applying for grants; now, we'll spend another month filling out more forms. And the forms don't protect anybody—they just take more time."

Even so, the molecular biologists at Asilomar were the first modern researchers to assume voluntarily some measure of social responsibility for their work.

Perhaps it is that the life sciences have come later to their crisis of responsibility. "Physics is checkers," a biologist once told me; "biology is chess." Even the terrible notion of biologic warfare has never really been a particularly efficient way to commit violence. It's simply too uncontrollable.

In a sense, then, the biologic sciences have only now suffered their first real loss of innocence: out of Mendel's monastery garden, so to speak, and into J. D. Watson's stainless steel laboratory.

And the box is only just opened. An antique science fiction story comes to mind that describes a military plague that drops upon a city, propagates briefly, infects all within and then — bacterial generations later — destroys itself, just as the conquering forces march in unscathed.

Pure science fiction. Yet only a few months ago, the top molecular biologists on the planet met to discuss, precisely — but benignly — how one might artificially create microorganisms programmed to self-destruct.

What is not science fiction, however, is that when artificial control of the evolutionary process—this "creation of novel biotypes never seen before in nature" — comes more firmly into our grasp, it will represent as profound an expulsion from the Garden as human intelligence has thus far managed. We will finally—on a molecular level — have cut ourselves loose from the dictates of primal nature. And at that point we will need all the foresight and self-control that we can muster.

And perhaps that was the final, foggy significance of Asilomar: a promise that the scientists who deal with the most fundamental of life stuff will not sequester themselves beneath Chicago stadiums or within blockhouses in the New Mexico desert — that their work, at least as significant as the most subtle of subnuclear manipulations, will be done with care and public scrutiny.

The territory, God knows, is uncharted. Not until late in the afternoon in that gilt San Francisco hotel room — deep in the midst of guidelines for experimental DNA recombination—does one middle-aged woman, staring intently at her working paper, abruptly begin to laugh.

The other panel members look up, puzzled.

"Do you realize," she says finally, "what this *means*?"

No one seems quite certain.

"This means," the woman announces brightly, "that we have just made human sex a moderate-risk experiment."

There is brief silence, then tentative laughter around the table.

"But that's only," someone else notes a moment later, "in the *laboratory*."

Revisions ensue immediately.